# BULLETIN
## OF
# THE JOHNS HOPKINS HOSPITAL

(THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL)

(SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY)

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July, 1933

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# RENAL INFECTIONS ASSOCIATED WITH PROSTATIC OBSTRUCTION[1]

HUGH H. YOUNG, M.A., M.D., D.S.M., F.R.C.S.I.

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*From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital*

Received for publication June 1, 1933

Infections of the kidney and other portions of the urinary tract form very important complications of prostatic obstruction; in fact, they are responsible, as either the primary or the secondary cause, of a large percentage of the mortality in prostatic cases. The most important predisposing cause of renal infections is the obstruction to the outflow of urine from the ureters into the bladder. In this the trigone plays a very important part. It is not generally realized, and is, in fact, not mentioned in the textbooks of physiology, that one of the most important functions of the trigone is to draw open the prostatic orifice, and thus to initiate the act of urination. We called attention to this fact in 1917 (1) as a result of cystoscopic studies, in which we showed that at the beginning of urination the trigone contracts violently, and thus pulls down the posterior margin of the prostato-vesical orifice, allowing the urine to rush from the bladder into the posterior urethra, while it is urged on by the contraction of the intrinsic muscles of the bladder. The combination of these forces brings about a violent desire to urinate, usually accompanied by immediate opening of the external voluntary sphincter, and completion of the urinary act. We published an extensive series of colored urethroscopic pictures, which demonstrated the opening of the sphincter, and the important part played by the lateral muscles, which are easily seen through the urethroscope, on each side, and which act to keep the internal orifice closed. These muscles (fig. 1) hold the posterior part of the prostatic margin, which has been called the uvula vesicae, forward against the anterior margin of the orifice, and thus

[1] Read before the annual meeting of the Association of Surgeons of Great Britain and Ireland, at Bristol, England, May 2, 1930.

close the "vesical sphincter" (2). In a very careful series of dissections and anatomical studies, Wesson verified my clinical observations and presented excellent illustrations of the anatomy of the vesical neck, and the correlation between the muscles constituting the internal

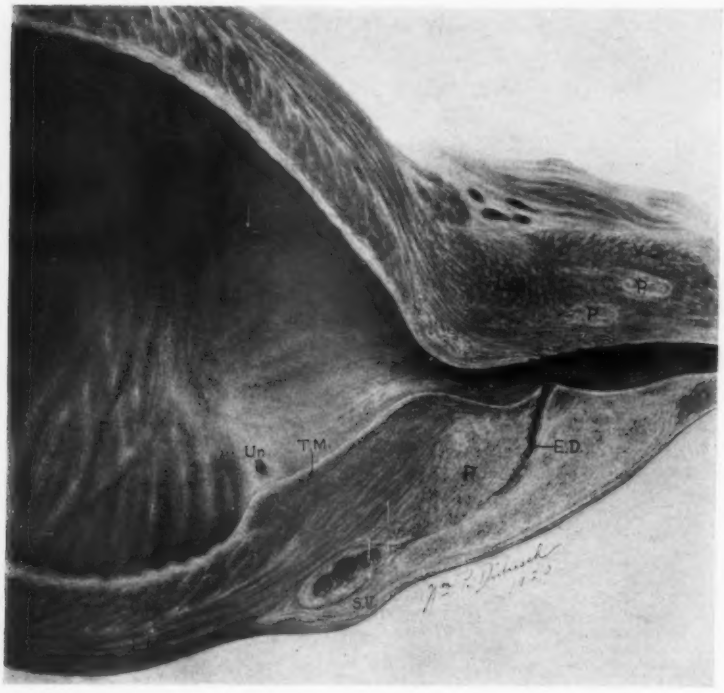


FIG. 1. SAGITTAL SECTION THROUGH BLADDER AND URETHRA IN MEDIAN LINE

The trigonal muscle is shown running down beneath the vesical orifice into the urethra. When this contracts, the urethral orifice is pulled downward and opened.

sphincter and trigone, the functioning of which had been seen by us, with the aid of the cystoscope and the endoscope. Macht (3), of our clinic, also furnished neurologic and pharmacologic confirmation of the physiology (see fig. 2). When obstruction at the prostatic orifice,

due to hypertrophied lobes or to bars or contractures, occurs, the trigone has to assert greater force in order to pull the prostatic orifice open, and if there is a middle lobe present, this entails great work on the trigone. As a result the trigone hypertrophies; in fact, this is one of the early signs of prostatic obstruction (fig. 3) and may be present before much enlargement is made out with the finger in the rectum, or with the cystoscope and the urethroscope. When this trigonal hypertrophy is combined with distinct trabeculation of the bladder, it may usually be accepted as definite evidence of obstruction, even though the prostate may seem normal. Furthermore, with the hypertrophy of the trigone, other important effects

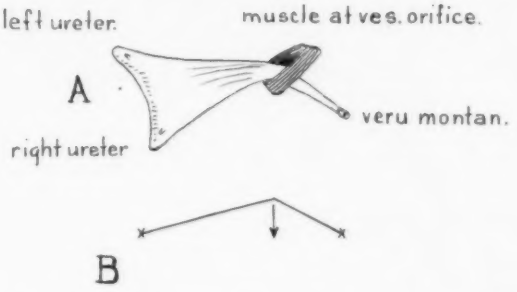


FIG. 2. DIAGRAM SHOWING MECHANISM BY WHICH CONTRACTURE OF THE TRIGONE OPENS THE VESICAL "SPHINCTER" (*A*). *B* SHOWS THE RESULTANT EFFECT OF CONTRACTURE OF THE ARCHED TRIGONE AND ITS INTRUSION INTO THE URETHRA

upon the ureters are produced. In his original paper describing the trigone, Bell said that it furnished the sphincters of the ureter, whose function it was to prevent reflux from the bladder up the ureter. He failed to recognize its very important work at the vesical orifice, and no one else has since detected this great and most important function of the trigone. During the urinary act, while the trigone is in contraction, holding open the vesical orifice, the ureteral orifices are closed, and during this brief period there is stasis of urine in the ureters, and interference with the regular peristaltic action, which carries urine from the kidney pelvis into the bladder. If urination is very frequent, this may result in dilation of the ureters. Thus we see in

cases of cystitis without prostatic obstruction, marked dilation of the ureters and kidney pelves. In addition to the increasing frequency of urination, if the urinary act is prolonged, as in prostatic obstruction, the interference with peristalsis, resulting in stasis and abnormal accumulation of urine at frequent intervals, leads inevitably

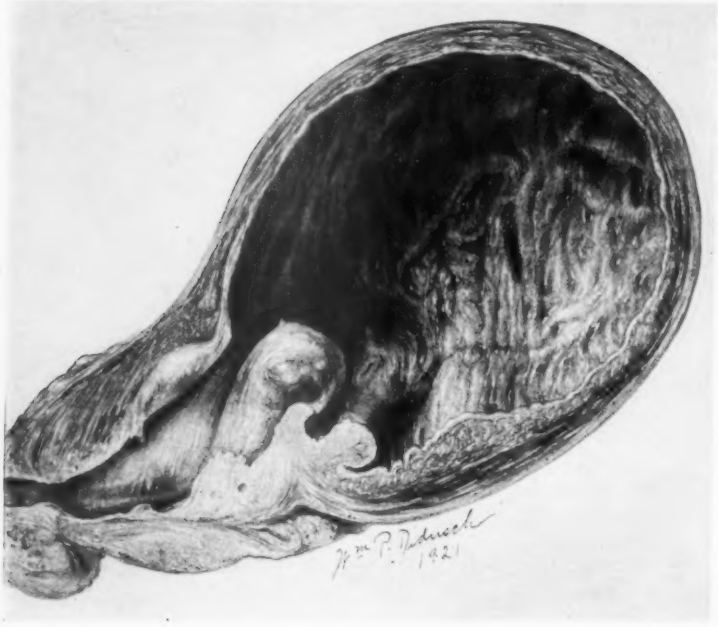

FIG. 3. SAGITTAL SECTION IN CASE OF PROSTATIC HYPERTROPHY, WITH CONSIDERABLE ENLARGEMENT OF LATERAL AND MEDIAN LOBES

The prostatic orifice was irregularly dilated. Trigone markedly hypertrophied, with pouch behind it.

to dilation of the ureters, kidney pelves, calices, and ultimate thinning of the renal cortex, which may progress until the kidney is a mere shell. Figure 4 shows the effect of this prostatic obstruction upon the upper urinary passages. Along with such back-pressure effects there occurs a gradual reduction in the function of the kidneys, acompanied

by an increasing accumulation of substances in the blood, tissues and organs, which normally should be eliminated. Vascular and cardiac changes of increasing importance occur, often characterized by high blood pressure, and causing damage to the myocardium. At the same time increasing evidence of uremia is usually present, with gastrointestinal and cerebral symptoms—a combination of the effects of the urinary back-pressure. We have not the space here to discuss

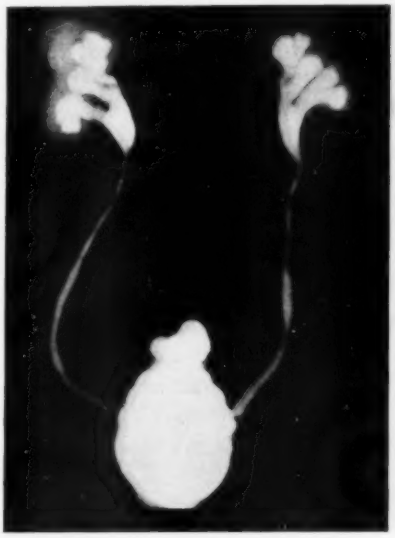

FIG. 4. Case of prostatic hypertrophy, with severe back-pressure effects; low phthalein, high blood urea. Postmortem injection of bladder with sodium iodide. X-ray showing reflux, dilated ureters, pelves and calices.

the very important systemic effects which such important changes in vital organs bring about, nor is it necessary to discuss at any length how such lesions predispose to infections, particularly of the upper urinary passages, thus greatly reduced in their vascularity, functional ability and resistance to infective agents.

In the examination for prostatic hypertrophy it is important to bear in mind the effects resulting from back-pressure of accumulated urine,

and to avoid doing anything which will precipitate a crisis. Before passing a catheter it is important to palpate and percuss the abdomen carefully, in order to detect any marked distention of the bladder. If the bladder, immediately after urination, is distended up to the umbilicus, as a rule, 1000 to 1200 c.c. of residual urine are present, and distension to half way between the umbilicus and pubes generally means 600 c.c. of residual urine. The bladder may be even much more distended. We have recently seen a case where it reached the ensiform, and probably contained at least 6,000 c.c., although the patient was still voiding naturally and at not very frequent intervals. Before we realized the importance of not emptying too rapidly such an overdistended bladder, we frequently saw catheterization immediately followed by a crisis and a violent drop in blood pressure, followed by suppression of urine and hemorrhage from the mucous membrane of the bladder and kidney pelves. Very early in our work we pointed out the great importance of drainage in combating the impairment of kidney function and uremia, but more recently we have realized the great importance of gradual decompression of these overdistended bladders (4) and have introduced a handy apparatus, by which this can be accomplished, after determining accurately the pressure upon which the bladder has been working, and gradually lowering this pressure until the organ is emptying itself freely (see fig. 5). When such a case, with considerable residual urine, is encountered, it is impossible to carry out the phenolsulphonphthalein test until the bladder is emptying itself freely through the catheter drain. Until such time, one has to rely on blood chemistry to determine whether the kidneys are badly impaired. We usually estimate the blood urea by a technique which is simple and accurate. The non-protein nitrogen furnishes no more information, and tests for creatinin and other substances are much less satisfactory than the blood urea.

But blood studies will not detect renal impairment in the early stages and it is here that the phenolsulphonphthalein test is of extreme importance. It may be undertaken at once in all cases with a small amount of residual urine, and in the case of copious residual urine, as soon as decompression has been effected. We have recently improved the technique of phenolsulphonphthalein examinations, particularly in the matter of recording them. We now use a chart in

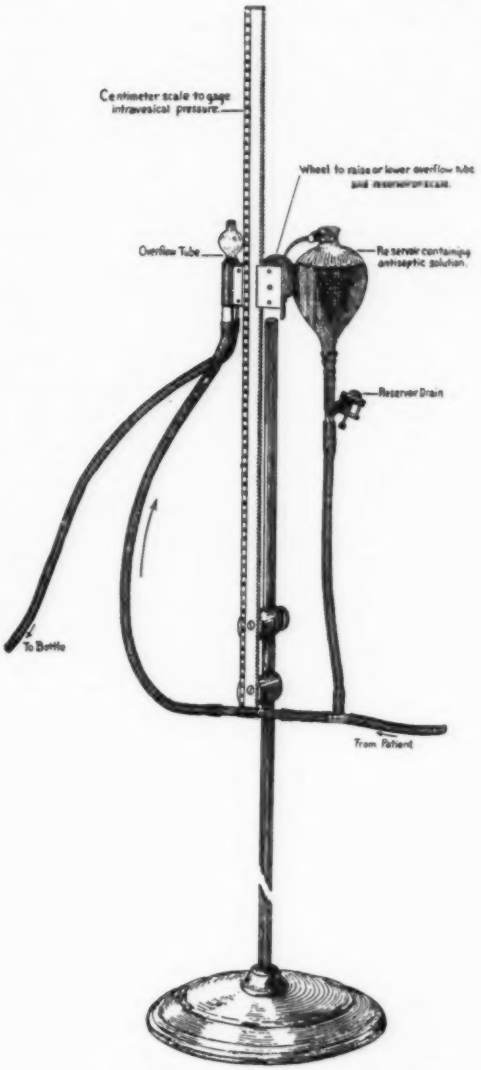
Centimeter scale to gage intravesical pressure.
Wheel to raise or lower overflow tube and reservoir as a unit.
Overflow Tube
Reservoir containing antiseptic solution.
Reservoir Drain
To Bottle
From Patient

FIG. 5. DECOMPRESSING MANOMETER USED IN GRADUAL REDUCTION OF HIGH RESIDUAL URINE

which is put down the appearance time of the phthalein (the number of minutes after injection before the drug appears in the alkalinized urine), the percentage eliminated or excreted every half hour for two hours after injection, and also after its appearance. Such a record is shown in figure 6, which depicts graphically the excretion of the phthalein, its comparison with the known normal and the improvement, under catheter drainage, from day to day. On the same chart the blood urea, non-protein nitrogen, creatinin, and other tests may also be recorded in milligrams per 100 c.c. These two charts often furnish a remarkable inverse parallelism, which shows at a glance an improvement in the kidney under the treatment employed. We have found it very helpful in the evaluation of the patient's condition in the management of the treatment, and for determining the time when operation may be safely carried out in cases of prostatic obstruction. I do not hesitate to say that without functional studies accurate prostatic surgery cannot be satisfactorily practised. It is not sufficient simply to depend upon the blood chemistry, which, as was said above, detects only the gross and serious lesions in the kidney. There may be marked impairment, which can be greatly benefited by preparatory drainage, without any changes in the blood demonstrable by blood chemistry. It is not possible by the constant of Ambard to arrive at any accurate conclusions. Certainly this test has been thoroughly discredited by many careful observers, and as Marion has recently remarked, "How many prostatics are dead because they had the misfortune to have an excellent constant!"

Of all the color tests, phenolsulphonphthalein is by far the best. Certainly no dependence can be placed on indigocarmine, only 25 per cent. of which is eliminated through the kidneys and far less rapidly than phthalein all of which is eliminated by the kidneys.

In prostatic obstruction, infections of the upper urinary tract may reach the pelvis by passing from the bladder up the ureter. This may be due to direct extension from the vesical mucous membrane to that of the ureter, or by infection from the bladder through the ureteral orifice to the urine retained by stasis in the ureter; or it may be incidental to a definite reflux. This is demonstrable in cystograms by the shadow which extends from the bladder up one or both ureters. In such cases the infection starts as a ureteritis and later involves the

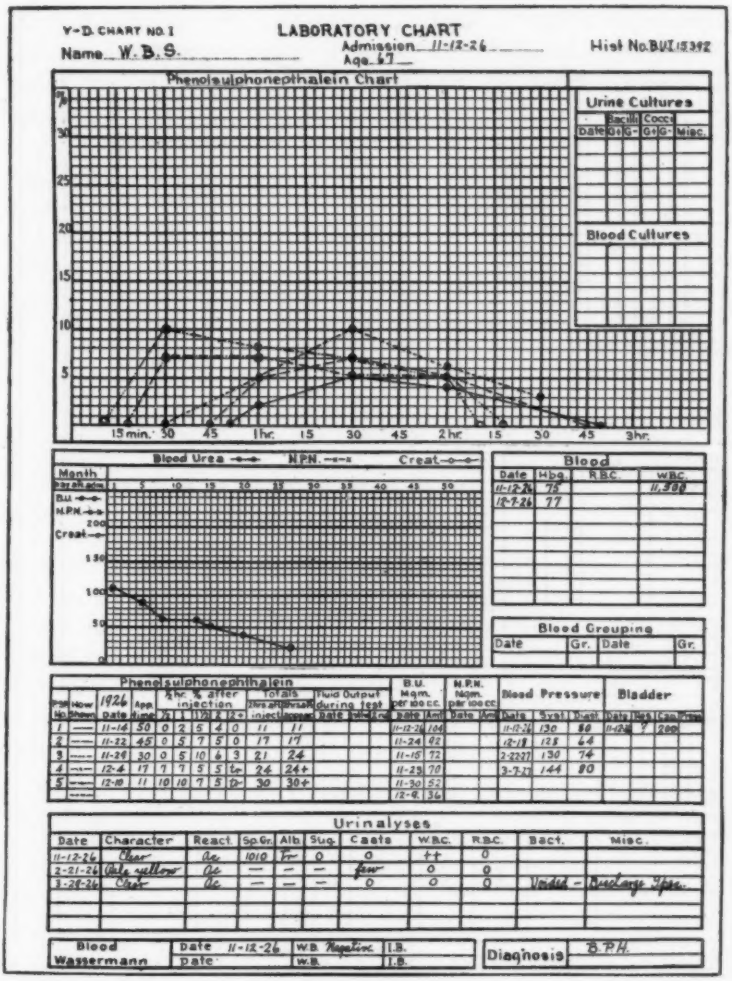


FIG. 6. Y and D. Chart I used in a case of benign prostatic hypertrophy with marked back-pressure effects, very poor phthalein and high blood urea, as shown in tabulations. Gradual improvement in renal function, as shown by phthalein chart, and steady fall in the blood urea. On admission the appearance time was 49 minutes and the curve (solid line) very poor; blood urea 110.

pelvis and calices. It may extend no farther, but frequently it extends into the tubules of the kidney and pyelonephritis results. Infection may reach the kidney also by the lymphatics accompanying

| PREDISPOSING FACTORS | LATER COMPLICATIONS | INFECTING ORGANISM | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | | Colon group | Gram cocci | Paratyphoid group | Proteus | Pyocyaneus | Number | Per cent |
| Lithiasis, hydronephrosis | 0 | 1 | 3 | 2 | 0 | 0 | 6 | 12 |
| Lithiasis, hydronephrosis ureteral stricture | 0 | 3 | 0 | 0 | 0 | 0 | 3 | 6 |
| Stricture, ureteral hydronephrosis | 2 with B. P. H. | 0 | 2 | 1 | 0 | 0 | 3 | 6 |
| Hydronephrosis, primary | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Ureteral stricture only | Ureteritis | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Lithiasis only | 1 prostatitis; 1 perinephric abscess | 4 | 7 | 1 | 3 | 1 | 16 | 32 |
| Prostatic Hyp. | 1 hydronephrosis | 2 | 0 | 0 | 0 | 0 | 2 | 4 |
| " " | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Median bar | Interstitial cystitis | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Gonorrhoea | 1 prostatitis; 1 hydronephrosis | 3 | 1 | 0 | 0 | 0 | 4 | 8 |
| C. N. S. lues | Prostatitis | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Epididymitis | 0 | 2 | 0 | 0 | 0 | 0 | 2 | 4 |
| Polycystic kidney | Prostatitis | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| Tonsillitis ? | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| 0 | Prostatitis or epididymitis | 4 | 0 | 0 | 0 | 0 | 4 | 8 |
| 0 | 0 | 2 | 0 | 1 | 0 | 0 | 3 | 6 |
| Total..... | | 28 (56%) | 13 (25%) | 5 (10%) | 3 (6%) | 1 (2%) | 50 | |

FIG. 7. AN ANALYSIS OF 50 CASES OF NON-TUBERCULOUS RENAL INFECTION

the ureter, or by the more general retroperitoneal system of lymphatics. Finally, renal infection may result from the transmission through the blood stream of bacteria present in infections of the urethra, pros-

tate and bladder. In an extensive series of bacteriological studies of the blood following urethral chills we have obtained at the Brady Urological Institute positive blood cultures in a large percentage of the cases. This work has been exhaustively treated by Scott in a recent publication (5). In the process of the elimination of these bacteria, infection may take place in the upper urinary passages, and sometimes localized abscesses in the cortex of the kidney, or in the tissues around the kidney, perinephric infection, abscess, etc., may result. The infection may remain unimportant, or go on to progressive injury, and even to final complete destruction, pyonephrosis, etc. Studies by J. H. Hill of our staff have shown that a great variety of bacteria may take part in these urinary infections, as shown in the accompanying tabulations. Figure 7 shows the results of bacteriological examinations in 50 cases.

An analysis of 50 cases of non-tuberculous renal infection shows that 56 per cent. of them were due to organisms of the Colon group. The relatively high incidence of strains of the B. lactis aërogenes group (Genus aerobacter) in urological infections is of clinical significance because of the greater resistance of these encapsulated organisms, both to the body defenses and to treatment. Although these organisms are commonly considered non-pathogenic, in the genito-urinary tract they are recovered in pure culture from many types of lesions and here are unquestionably pathogenic. They appear in the blood stream in urological cases more frequently than any other organism.

Gram-positive cocci were responsible for 26 per cent. of this series of 50 cases of renal infection. Thorough bacteriological study of 15 strains of Gram-positive cocci obtained in pure culture from 15 cases of renal infection has recently shown that 5 of these organisms were Staphylococcus aureus, 1 Staphylococcus citreus, 2 Staphylococcus albus, 1 Streptococcus and 6 miscellaneous strains, which it has been impossible to identify by available methods. It seems probable, according to J. H. Hill, that just as our ideas in relation to the pathogenicity of members of the colon group for the genito-urinary tract are being modified, so we may eventually obtain more valuable knowledge than we have at present in regard to these cocci. The inadequacy of present ideas of pathogenicity of these organisms is shown

by the fact that out of 18 pure strains of Staphylococcus aureus obtained from urine, only 10 were pathogenic for the patients from which they were obtained, while, on the other hand, many of the white, incompletely described organisms have been shown to have very marked pathogenicity for the kidney or prostate.

| TYPE OF ORGANISM IN BLOOD | TOTAL NUMBER OF CASES | PRE-OPERATIVE BLOOD INVASIONS | POST-OPERATIVE BLOOD INVASIONS | BOTH PRE- AND POST-OPERATIVE BLOOD INVASIONS | DEATHS DUE TO ORGANISMS | DEATHS DUE TO OTHER CAUSES | CASES APPARENTLY CURED BY INTRAVENOUS MERCUROCHROME |
|---|---|---|---|---|---|---|---|
| B. lactis aërogenes group (Aerobacter) | 9 | 2 | 6 | 1 | 1 | 0 | 2 |
| B. coli group (Escherichia) | 6 | 1 | 5 | 0 | 0 | 1 | 2 |
| Staphylococci | 4 | 0 | 4* | 0 | 2 | 1 | |
| Proteus | 2 | 0 | 2 | 0 | 0 | 1 | |
| B. pyocyaneus | 2 | 1 | 1 | 0 | 0 | 0 | |
| Paratyphoid group (Salmonella) | 1 | 0 | 1 | 0 | 0 | 0 | |
| Typhoid group (Eberthella) | 2 | 1 | 1 | 0 | 0 | 0 | |
| Mixed cultures | 3 | | | | | | |
| Proteus and Aerobacter | | 0 | 1 | 0 | 0 | 1 | |
| Proteus and a coccus | | 0 | 1 | 0 | 1 | 0 | |
| Eberthella and a coccus | | 0 | 1 | 0 | 1† | 0 | ‡ |
| Varying cultures | 2 | | | | | | |
| Strept. pre-oper., B. pyocyaneus post-oper | | 0 | 0 | 1 | 0 | 1 | |
| Eberthella and a hemophilic bacillus | | 0 | 1 | 0 | 0 | 0 | |

* One punch.

† Pneumonia.

‡ Temporarily improved.

FIG. 8. THIRTY-ONE CASES OF BLOOD-STREAM INVASION ASSOCIATED WITH BENIGN PROSTATIC HYPERTROPHY

In this series of 50 cases, 10 per cent. of the infections were due to organisms of the paratyphoid group (Genus salmonella). A larger series would undoubtedly show organisms of the typhoid group (Eberthella) and the dysentery group (Shigella). These many intermediate forms which occur in urological infections are of the greatest

interest biologically, since they provide connecting links between the arbitrarily defined genera at present available for classification.

Of the cultures in this series 6 per cent. were Proteus. All 3 of the proteus strains were associated with lithiasis. In 1 case B. pyocyaneus was obtained in pure culture from a kidney. This organism presents serious difficulties in the genito-urinary tract, because of its extreme resistance to treatment.

An analysis of 31 cases of blood-stream invasions associated with benign prostatic hypertrophy has been made by L. R. Seidman of this clinic. It was found that members of the B. lactis aërogenes group (Aerobacter) cause more of these invasions than any other group of organisms; in fact 9 of the cases, or about 30 per cent. of the total series, were due to these bacilli. This confirms the earlier findings of Hill, Seidman, Stadnichenko and Ellis of this Institute (6). The colon group as a whole cause 50 per cent. of the blood-stream invasions. Figure 8 shows the incidence of other organisms in these blood-stream invasions. Although the series is too small to allow the drawing of statistical comparisons, the fact that in 5 of the 31 cases death was directly due to the organisms found in the blood stream may be noted.

## TREATMENT

*Preventive.* Asepsis, rigid in its exactions, is the most important preventive treatment which may be employed. Catherization, as a rule, is much too carelessly carried out. Not only should the instruments be boiled, but the urethra and the genital organs should be thoroughly cleansed and treated with an antiseptic. An antiseptic towel should cover the parts during instrumentation, and the hands of the operator should be sterile. Unfortunately, such is not usually the case, and one sees in many clinics the most careless methods of catheterization in vogue. Drinking large quantities of water keeps the urinary passages flushed and hinders infection, and this is probably one of the most important preventive measures. Unfortunately, the use of large quantities of water prevents the working of internal antiseptics, most of which depend on a concentrated acid urine to exert a valuable influence upon the flow excreted. To give urotropin, acriflavin, mercurochrome and other oral antiseptics along with large

quantities of water is useless. If internal antiseptics are employed, it is well, not only to reduce the amount of fluid given, but to give the patient fairly large doses of acidifying drugs, such as acid sodium phosphate, in order to assist in the elimination of the drug in antiseptic strength in the upper urinary passages. Where the infection has become more pronounced, or is accompanied by definite evidence of serious kidney lesion, more active measures, such as the intravenous administration of antiseptics, or possibly surgical interference,

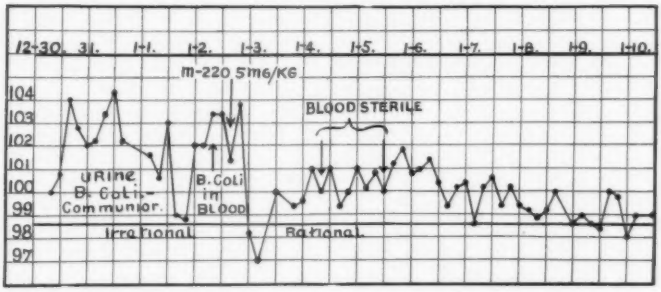


FIG. 9. Man, aged 44 years. Double pyelonephritis following ureteral catheterization. General septicemia. B. coli. One hundred and forty colonies per c.c. blood. Temperature varied from 103° to 104°. On January 3, 1922, patient was irrational. Medical consultants thought the case hopeless, and patient would not live more than a few hours. Mercurochrome, 1 per cent., 34 c.c. intravenously (5 mg./kg. of patient's body-weight). Injection was followed by chill, slight rise in temperature and precipitate drop of 6 degrees in about four hours. Blood culture twelve hours after injection sterile. Patient had become conscious and was greatly improved. Ate breakfast. Rapid convalescence. Blood cultures remained sterile. Patient was discharged well in seven days.

are to be considered. The methods which we usually employ are as follows:

All prostatic patients are given large amounts of water to drink, and if they are unable to take it by mouth, they are given water by rectum, and by hypodermoclysis. If uremia is present, it is usually advisable to employ injections of salt or 5 per cent glucose intravenously in addition to the other routes. In the majority of cases, when there is a mild infection present, evidenced by slight symptoms localized

in the region of the kidney, a moderate fever and pain, the water cure, as above outlined, may prove sufficient. If, however, the fever is more pronounced, infection more evident, and the pathological condition more definite, we usually employ intravenous medication. In 1923 we demonstrated for the first time (7) that in a case of bilateral pyelonephritis complicated by grave septicemia, with 140 colonies

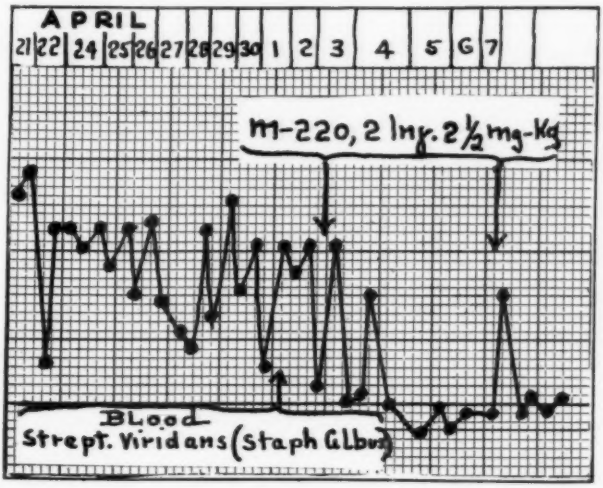


FIG. 10. Female, aged 25. Admitted with infectious nephritis and acute secondary pyelitis due to B. coli, was cleared under pelvic lavage, but the general condition of the patient became worse, resembling a mild typhoid state. Blood culture showed Streptococcus viridans; white blood count varied from 9,000 to 37,000. Mercurochrome intravenously two injections, 2.5 mg./kg., marked improvement following the first injection. Permanent drop in temperature; rapid and uninterrupted recovery after the second injection. Personal communication, Dr. T. Baker, Pittsburgh, Pa.

of B. coli to the centimeter of blood, it was possible to sterilize the blood promptly, and indeed to cure the renal infection, by a single intravenous injection of 34 c.c. of a 1 per cent. solution of mercurochrome, as shown in the accompanying chart (Fig. 9). Since then we have employed intravenous therapy in hundreds of cases in which urinary infection, with or without septicemia, was present. Some

of these cases are shown in the accompanying charts (Figs. 10, 11, 12, 13 and 14) with legends which give brief clinical notes.

As a result of many thousands of intravenous injections of 1 per cent. mercurochrome, we may now state that the method is not dangerous; that smaller doses are often as effective as the larger doses which we at first employed. We now usually begin with 10 c.c. of a 1 per cent. solution, and after an interval of a day or two, increase the

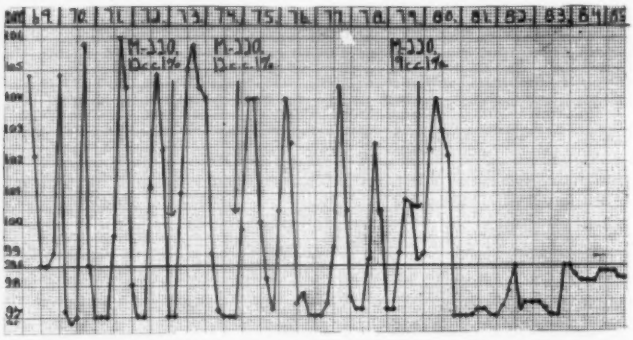

FIG. 11. Female, aged 17, admitted University of California Hospital, April 10, 1924, with illness of two months' duration, during which there had been chills, fever, skin rash, swollen and painful joints, suppurative gland back of the left ear, cultures from which yielded streptococci. White blood count, April 24, 20,500. Urine hyaline casts and Streptococcus hemolyticus. Temperature continued of the septic type indicated until April 23, when the first intravenous injection of mercurochrome, 12 c.c., 1 per cent. was given, followed by a second dose, April 29. Following this, there was an immediate drop in temperature below normal. Patient was discharged well in nine days, and so continued under observation. The exact cause of the general infection could not be determined, but the long-continued fever disappeared after the third injection of mercurochrome. Case of Dr. F. H. Kruse, San Francisco.

dose 3 c.c., and, if necessary, after intervals of two or three days, give an additional injection, increasing the dosage 2 or 3 c.c. each time (only rarely are more than 4 or 5 intravenous injections necessary); that in fulminating cases the original dose of 5 mg./kg. (23 c.c. of a 1 per cent. solution per 100 pounds of body-weight) is desirable; that the treatment does not produce nephritis, or more than transient

albuminuria and intestinal irritation; that the results are better in acute than in chronic cases (low grade B. coli infections of the upper urinary passages being the most resistant); that staphylococci are usually eliminated quickly, both mercurochrome and novarsenobenzol being particularly effective in getting rid of such infections; that almost every type of organism has been eliminated by intravenous injections of mercurochrome; that within a few minutes after intra-

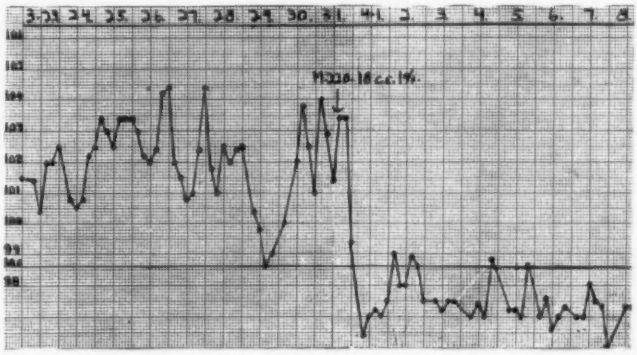

FIG. 12. B. U. I. 13262. Male, aged 61. Admitted to this clinic with diagnosis of benign prostatic hypertrophy. Perineal prostatectomy, after which progress was good until seventeenth day, when septic temperature began, which continued, accompanied by left pyelonephritis for fourteen days, at the end of which time the patient received intravenous mercurochrome, 18 c.c., 1 per cent., followed by chill and drop of temperature to below normal. The sepsis and pyelonephritis were completely terminated, although the urine remained infected. Urine on admission: cocci 2 plus, bacilli 2 plus, albumin trace, no casts, pus 2 plus, PSP. for two hours 37 per cent.; 30 per cent. the first hour. On discharge urine showed a few cocci, bacilli 2 plus, albumin trace, no casts, pus 2 plus; PSP. first hour, 68 per cent. Case of Dr. J. A. C. Colston.

venous injection of mercurochrome, the drug appears in the urine; within an hour it is found present in strongly inhibitive concentration, and in some cases, when the amount of fluids is limited, distinctly bactericidal urine is produced; that it is usually desirable to give the patient local treatment of the urinary passages—urethra, bladder and ureters—in most cases of pyelitis.

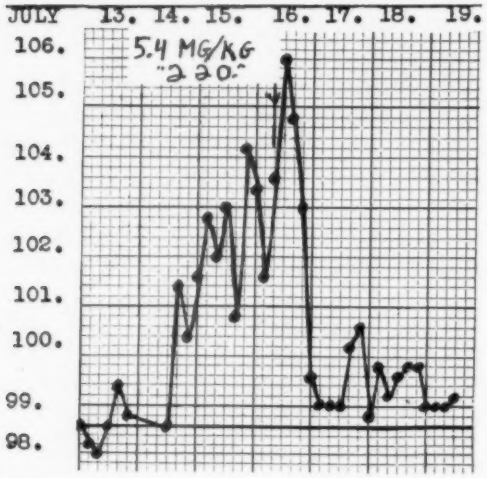


FIG. 13. Youth, aged 17 years. Hypospadias. Plastic operation. Three weeks later, following instrumentation of urethra and bladder, chill and fever which rose in three days to 104°. A large, tender mass developed in the left side. Diagnosis retroperitoneal perinephric abscess. Cultures from urine, B. coli. It was decided to see what intravenous mercurochrome would do; 27 c.c. 1 per cent. solution intravenously (5.4 mg./kg). Severe chill; in twelve hours temperature dropped to 99.6° (7 degrees). Patient was free from pain. Muscle spasm and mass disappeared rapidly. Patient got well without operation. Urine became sterile.

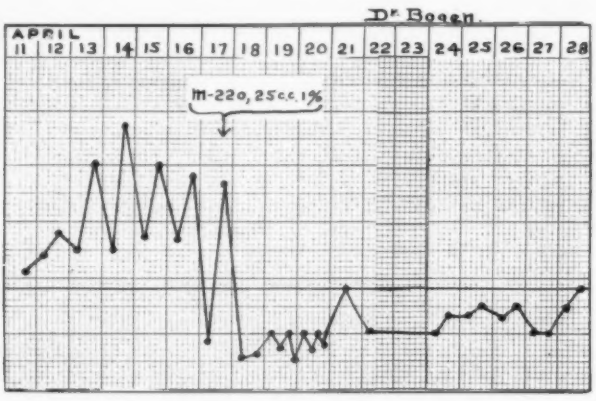


FIG. 14. Erysipelas, mastoiditis, sepsis; condition very grave. Striking benefit from mercurochrome—220, one injection, 25 c.c., 1 per cent.

By this combination of local and intravenous treatment, a cross-fire attack is effected, which is valuable in all types of genito-urinary infections, including those due to the gonococcus (in fact, we now employ both local and intravenous treatment in all cases of gonococcus infections) and as a result have been able to clear up promptly many long-standing deep-seated gonococcal invasions by this method. That there have been many failures in intravenous antiseptic therapy with mercurochrome, as with other drugs, I do not deny, but on the other hand, there have been many successes which have far outweighed the failures. Over 70 per cent. of the septicemia patients have recovered in a series of over 300 cases, and many other general and local infectious conditions have apparently responded to intravenous medication. The most discouraging, as stated above, have been the chronic, low grade B. coli infections, but even here a good many splendid results have been obtained.

In closing it may be stated briefly that renal infections associated with prostatic obstruction are not very common. They can usually be prevented by hypodermoclysis, drainage and antiseptic treatment of the lower urinary passages. Taken at the beginning, hydrotherapy is usually alone sufficient. When associated with fever, and particularly if accompanied by bacteremia or definite septicemia, intravenous therapy is imperatively indicated. For this purpose, several drugs are at hand, but in our opinion the most reliable is mercurochrome, introduced in 1 per cent. solution in doses of from 10 c.c. upward at intervals of from one to three days. By means of careful clinical and laboratory studies, an accurate evaluation of the renal conditions present and of the preliminary treatment necessary, of the stage at which it is safe to operate, and how to carry the patient through a successful convalescence, can be determined with almost mechanical precision. Such methods have resulted in reducing the mortality rate in cases of prostatic obstruction to almost nil in several clinics.[2]

[2] A recent study of the patients upon whom the author himself has operated during the past twenty-five years shows 1571 cases with 58 deaths, a mortality of 3.6 per cent. We have recently had one period of 3 years and 6 months during which there were 198 consecutive perineal prostatectomies without a death.

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# THE EFFECT OF INSULIN INJECTIONS UPON THE SERUM INORGANIC PHOSPHATE IN NORMAL AND SUPRARENALECTOMIZED DOGS

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In 1924, Harrop and Benedict (1) reported that the injection of insulin in normal and diabetic subjects was followed by a fall in inorganic phosphate of the blood. This finding was confirmed by Wigglesworth and others (2) in a paper that appeared shortly thereafter. Subsequently this phenomenon has been observed many times (3) (4) and it is now well known. In the experiments of Harrop and Benedict, the fall in serum inorganic phosphate was accompanied by a transient diminution in urinary phosphate. Later there was a rise in phosphate excretion, so that the 24-hour output was about normal. This was clearly confirmed by Sohkey and Allen (5) and by Blatherwick, Bell, and Hill (6). Harrop and Benedict found an increase in the total phosphate and in the "organic" phosphate content in rabbit muscle after insulin. In view of recent developments of our knowledge of the phosphorus compounds of muscle, and because of criticisms of all older methods for estimating the various forms of phosphate present there, it is not possible to be sure what fraction of muscle phosphate was found to be increased by Harrop and Benedict. We can, however, accept their demonstration of an increase in the total phosphate of muscle after insulin injection.

Harrop and Benedict further demonstrated that the ingestion of glucose caused a drop in the serum inorganic phosphate. Fiske (7) had previously found that carbohydrate feeding was accompanied by a temporary decrease in urinary phosphate. The supposition of Harrop and Benedict, that the fall in inorganic phosphorus of the blood and urine after glucose might be associated with mobilization of insulin in response to the carbohydrate ingestion, received support

when Bolliger and Hartman (8) and Markowitz (9) reported that in diabetic animals injection of glucose was almost without effect upon phosphorus excretion.

Perlzweig, Latham and Keefer (10) found that epinephrine injection also produced a fall in the serum inorganic phosphate. They reported changes in the urinary excretion of phosphorus after epinephrine administration similar to those which follow that of insulin.

Cori and Cori (11), devising a method for the estimation of hexose phosphate in muscle, which they believe to be free from the criticisms that cast suspicion upon the earlier results, have reported a rise in the hexose monophosphate of muscle after epinephrine and also after insulin. They assert that the accumulation of hexose monophosphate in muscle after epinephrine injection accounts for the known fall in serum and urine phosphate. Inasmuch as the hexose monophosphate of muscle of suprarenalectomized rats showed no change after insulin, they concluded that the fall in inorganic phosphate after insulin was due to a reflex discharge of epinephrine, elicited by the hypoglycemia. As the experiments were performed upon rats, they could not follow the changes in blood as well as those in muscle. The ingestion of glucose or of glucose and insulin (so that hypoglycemia was prevented) caused no change in muscle hexose monophosphate. The fall of the serum phosphorus, therefore, in this case remained unexplained.

It seemed to us that a comparison of the behavior of serum inorganic phosphate after insulin injection in the normal and the totally suprarenalectomized dog, maintained on cortical extract, might throw considerable light upon the part played by epinephrine in the explanation of serum phosphate behavior after insulin. The present experiments were devised to obtain that information.

The dogs used were divided into three groups: (1) normal, (2) unilaterally suprarenalectomized, (3) completely suprarenalectomized. The suprarenalectomized animals received amounts of cortical extract adequate to maintain them in excellent condition (Harrop and Weinstein (12)). They were not suffering from insufficiency of the suprarenal cortex at the time of the experiments. In effect, they represented, approximately, animals deprived only of the suprarenal medulla. Insulin, epinephrine and glucose were given intravenously

and the effect upon blood sugar and inorganic phosphate at various intervals thereafter was observed. The amounts of insulin, epinephrine, and glucose, weight of animals, times of blood sampling, and results of sugar and phosphate determinations are given in tables I

TABLE I

*Normal dogs; insulin 2 units per kilogram*

| F-7, WEIGHT 10.3 KG. | | | F-6, WEIGHT 7 KG. | | |
|---|---|---|---|---|---|
| Time | Blood | | Time | Blood | |
| | Sugar | Serum P* | | Sugar | Serum P |
| *minutes* | *mgm. per cent* | *mgm. per cent* | *minutes* | *mgm. per cent* | *mgm. per cent* |
| 0 | 87 | 2.9 | 0 | 86 | 3.8 |
| 73 | 32 | 1.3 | 58 | 32 | 1.4 |
| 124 | 35 | 1.3 | 124 | 25 | 1.9 |
| 182 | 37 | 1.3 | 179 | 20 | 3.0 |
| 303 | 73 | 6.1 | 301 | 50 | 7.1 |

* Throughout "Serum P" is abbreviation for "Serum Inorganic P."

TABLE II

*Dogs with one adrenal removed; insulin 2 units per kilogram*

| F-5, WEIGHT 11 KG. | | | F-4, WEIGHT 10.0 KG. | | | | F-3, WEIGHT 10.0 KG. | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time | Blood | | Time | Blood | | Remarks | Time | Blood | | Remarks |
| | Sugar | Serum P | | Sugar | Serum P | | | Sugar | Serum P | |
| *minutes* | *mgm. per cent* | *mgm. per cent* | *minutes* | *mgm. per cent* | *mgm. per cent* | | *minutes* | *mgm. per cent* | *mgm. per cent* | |
| 0 | 92 | 6.7 | 0 | 96 | 5.7 | Lying flat in | 0 | 84 | 4.5 | Convulsions. |
| 59 | 31 | 3.3 | 28 | 67 | 2.2 | cage, weak- | 72 | 24 | 1.6 | Given glu- |
| 121 | 35 | 3.5 | 58 | 18 | 1.5 | ness but no | 122 | 15 | 2.1 | cose 2.5 gm. |
| 178 | 39 | 6.4 | 120 | 13 | 2.7 | convulsions | 192 | 217 | 3.2 | i.v. and 20 |
| 301 | 45 | 8.3 | 240 | 28 | 7.6 | | 305 | 144 | 6.7 | gm. per os |

to V, in which are also recorded the occurrence of convulsions or other serious symptoms. It will be seen, that in several instances it was necessary to administer glucose and even epinephrine. As the drop in serum phosphate had taken place before any such medication was

TABLE III

*Bilaterally adrenalectomized dogs; insulin 0.5 unit per kilogram*

| NO. 15, WEIGHT 7.9 KG. | | | | NO. 13, WEIGHT 14.3 KG. | | | |
|---|---|---|---|---|---|---|---|
| Time | Blood | | Remarks | Time | Blood | | Remarks |
| | Sugar | Serum P | | | Sugar | Serum P | |
| *minutes* | *mgm. per cent* | *mgm. per cent* | | *minutes* | *mgm. per cent* | *mgm. per cent* | |
| 0 | 63 | 8.0 | | 0 | 78 | 4.2 | |
| 60 | 28 | 6.3 | | 50 | | | Convulsion |
| 70 | | | Convulsion | 58 | 29 | 2.0 | Glucose 4 gm. i.v. Glucose 20 gm. per os |
| 80 | | | Glucose 7 gm. i.v. | 142 | 31 | 1.4 | |
| 120 | 245 | 5.6 | | 201 | 31 | 1.3 | |
| 190 | | | Glucose 25 gm. per os. Epinephrine 0.5 mgm. | 305 | 22 | 5.4 | Animal survived well in spite of low Bl. sugar |
| 310 | | | Glucose 20 gm. per os. Epinephrine 0.5 mgm. | | | | |
| 390 | 540 | 19.0 | Last blood sample obtained immediately after death | | | | |

No. 13 had been adrenalectomized February 1931 and had been maintained on cortical extract since that time.

TABLE III—*Concluded*

*Dog 70, bilaterally adrenalectomized*

| WT. 9.5 KG. INSULIN* 0.5 UNIT PER KILOGRAM | | | | WT. 9.0 KG. INSULIN* 0.25 UNIT PER KILOGRAM | | | | WT. 8.7 KG. INSULIN* 0.125 UNIT PER KILOGRAM | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Time | Blood | | Remarks | Time | Blood | | Remarks | Time | Blood | | Remarks |
| | Sugar | Serum P | | | Sugar | Serum P | | | Sugar | Serum P | |
| *minutes* | *mgm. per cent* | *mgm. per cent* | | *minutes* | *mgm. per cent* | *mgm. per cent* | | *minutes* | *mgm. per cent* | *mgm. per cent* | |
| 0 | 80 | 6.0 | | 0 | 79 | 5.5 | | 0 | 75 | 6.0 | |
| 30 | 32 | 4.0 | Very quiet | 30 | 20 | 3.4 | | 30 | 35 | 4.3 | Very quiet |
| 50 | | | Convulsion lasting 2 minutes | | | | Convulsion | 60 | 25 | 4.3 | Comatose. Slight twitching occasionally |
| 60 | 27 | 4.6 | Comatose | Experiment terminated because of critical condition of animal | | | | | | | |
| 120 | 24 | 5.1 | Comatose | | | | | 120 | 27 | 5.2 | Comatose |
| 125 | | | 25 gm. glucose i.v. 20 gm. glucose p.o. 1 cc. epinephrine subcutaneously Animal responds | | | | | 160 | | | 10 gm. glucose i.v. 20 gm. glucose p.o. Dog responded immediately |
| 300 | 270 | 3.1 | Animal responds | | | | | 335 | 187 | 7.2 | Normal appearance |

* Crystalline insulin used. Kindly supplied by Dr. E. M. K. Geiling of the Department of Pharmacology.

given, in no case did the treatment interfere with the essential value of the results for purposes of the present discussion.

The serum inorganic phosphorus was estimated by the method of Fiske and Subbarow (13), the blood sugar by that of Folin and Wu (1929) (14).

TABLE IV

*Dogs with one adrenal removed*

| INSULIN 2 UNITS PER KILOGRAM GLUCOSE 2 GM. PER KILOGRAM F-7, WEIGHT 9.7 KG. | | | INSULIN 2 UNITS PER KILOGRAM EPINEPHRINE 0.001 GM. F-3, WEIGHT 10 KG. | | | |
|---|---|---|---|---|---|---|
| Time | Blood | | Time | Blood | | Remarks |
| | Sugar | Serum P | | Sugar | Serum P | |
| *minutes* | *mgm. per cent* | *mgm. per cent* | *minutes* | *mgm. per cent* | *mgm. per cent* | |
| 0 | 67 | 3.7 | 0 | 86 | 4.1 | |
| 30 | 107 | 2.9 | 27 | 51 | 2.4 | |
| 60 | 154 | 3.6 | 56 | 27 | 1.3 | Restlessness |
| 120 | 86 | 3.6 | 118 | 13 | 2.5 | No convulsions |
| 80 | 66 | 4.4 | 240 | 13 | 6.2 | |

TABLE V

*Dogs with one adrenal removed; adrenalin 0.001 gm.*

| F-3, WEIGHT 10 KG. | | | | F-4, WEIGHT 10 KG. | | | |
|---|---|---|---|---|---|---|---|
| Time | Blood | | Remarks | Time | Blood | | Remarks |
| | Sugar | Serum P | | | Sugar | Serum P | |
| *minutes* | *mgm. per cent* | *mgm. per cent* | | *minutes* | *mgm. per cent* | *mgm. per cent* | |
| 0 | 87 | 6.0 | Restlessness | 0 | 76 | 6.4 | Restlessness |
| 30 | 118 | 5.8 | Restlessness | 30 | 130 | 5.3 | Restlessness |
| 60 | 92 | 4.5 | Restlessness | 60 | 104 | 4.9 | |
| 120 | 86 | 4.7 | | 120 | 96 | 4.6 | |

## DISCUSSION

It is seen at once from the tables that the initial serum inorganic phosphorus values varied considerably. The figures for the unilaterally and bilaterally suprarenalectomized animals fell into the same range. Both sets were somewhat higher than the values obtained in

normal animals. An explanation of this we are not able to offer at present.

Following the injection of insulin, there was a pronounced drop in serum inorganic phosphate in all the animals. Here, again, some variation in the magnitude of response in the animals was observed. The important point is that, in the completely suprarenalectomized animals, a very decided fall in serum inorganic phosphate occurred after insulin. Regardless of the initial level, the decrease in serum phosphate in milligrams per 100 cc., which occurred during a given time after insulin injection, was approximately the same in the completely suprarenalectomized and in the normal animals. In the unilaterally suprarenalectomized animals the fall of serum phosphate was similar and slightly greater in degree. The observed drop in the serum inorganic phosphate of the completely suprarenalectomized animals is all the more remarkable, since these animals received only one-quarter to one-sixteenth as much insulin as the controls.

About the time of completion of these studies a report was made to the American Society of Biological Chemists by Cori and Cori (15) concerning some work with suprarenalectomized rabbits. In these they obtained no fall of serum phosphate after the intravenous injection of insulin.

It is difficult to reconcile their findings with ours, in all points, although a species difference in reaction may exist. The maintenance of our animals in good condition with cortical extract may have had a considerable influence and, moreover, they are not strictly comparable to the rabbits of Cori and Cori's experiments. Cori and Cori found also that the intravenous injection of glucose in normal fasting rabbits produced almost no fall in serum phosphate in two hours. This is contrary to the experience of Harrop and Benedict (1) with human subjects. Injection of glucose plus insulin, however, in the experiments of Cori and Cori, even in the suprarenalectomized rabbits, produced a fall in serum phosphate.

Everyone is agreed that epinephrine produces a fall in serum inorganic phosphate. Table 5 shows two fairly characteristic curves for the first two hours after epinephrine injection. As already mentioned, the accumulation of hexose monophosphate in muscle would seem to account for this (1) (11).

In regard to the fall in serum inorganic phosphate after insulin and the fall observed by Harrop and Benedict and others after glucose feeding, there is less agreement. Cori and Cori ascribe the effect of insulin to a reflex outpouring of epinephrine in response to the hypoglycemia. This, of course, would not explain the drop in serum inorganic phosphate after carbohydrate ingestion and that explanation would also imply that our suprarenalectomized dogs were able to mobilize epinephrine as rapidly as normal dogs. Furthermore, in the dog F-7 (table IV) there occurred a fall of serum inorganic phosphorus during a rise in blood sugar after glucose and insulin. A reflex epinephrine effect could not here be evoked in explanation, nor could it in the suprarenalectomized rabbits of Cori and Cori (15), in which a fall in serum phosphorus took place after glucose and insulin.

In regard to the mobilization of epinephrine we have been unable to obtain direct evidence to show whether a suprarenalectomized animal can or can not produce epinephrine from other chromaffin tissues, in response to hypoglycemia, as rapidly as the intact animal. However, it is well-known that suprarenalectomized animals are extremely sensitive to insulin. This is very well demonstrated in table III (dog 70). This suprarenalectomized animal reacted with severe and prolonged hypoglycemia to as little as one unit (one-eighth unit per kilo) of crystalline insulin. The extreme hypersensitivity of suprarenalectomized animals and particularly the prolongation of the hypoglycemia is usually considered as indirect evidence that the suprarenalectomized animal does not mobilize epinephrine as the normal.

This would strongly suggest that, while the major lowering of blood phosphate after insulin injection may be due to a reflex discharge of epinephrine, there is another mechanism following the administration of insulin or of glucose or both, which accounts at least in part for the observed fall of serum and urine phosphate.

One additional point we wish to make is that, after the preliminary fall, the phosphate curve rises above and often much above the normal level. This occurs usually between the third and fifth hour after insulin injection. Convulsions are known to produce an increase of phosphate in the blood, but the rise above the control level observed here occurred even in the absence of convulsions. We do not believe

this has been emphasized before. It would account very well for the compensating phosphorus diuresis which has long been shown to follow the temporary drop in urine phosphate excretion.

## SUMMARY AND CONCLUSIONS

1. Observations of the changes in serum phosphate and blood sugar in normal, in unilaterally suprarenalectomized and in completely suprarenalectomized dogs after insulin injections are reported.

2. The amount of fall in serum inorganic phosphate in a given interval after insulin injection was approximately the same in completely suprarenalectomized animals maintained on cortical extract as in normal animals.

3. The bearing of this upon the explanation of the phosphate fall after insulin is discussed.

4. It has been observed that, after the well-known fall in serum inorganic phosphate, there is a rise to a level higher and often much higher than the control value.

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# PHYSIOLOGICAL STUDIES FOLLOWING EXTIRPATION OF THE RIGHT CEREBRAL HEMISPHERE IN MAN

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Attempts to localize cerebral functions based upon the effects of cerebral tumors or degenerative processes—until recently the only sources for such information—have led to the most contradictory results, and for very good reasons. The disturbances caused by a brain tumor are not restricted to the region of brain tissue that it occupies. Indeed tumors very frequently induce symptoms in far distant parts of the brain either from contiguous cerebral oedema or from the transfer of intracranial pressure. Nor can the absence of signs or symptoms be taken as evidence of the absence of function of a given part of the brain when this region is occupied by a tumor, for encapsulated or well circumscribed tumors may merely push the brain aside without altering its function; and infiltrating tumors may surround, without destroying, cerebral tracts even though the gross appearance of the tumor would give every reason to believe that non-interference with functions was impossible. The net result of tumor analyses furnishes a seeming paradox, for some tumors in a given region produce no obvious loss of function, whereas others of the same size and in precisely the same location cause the most widespread and profound alterations in their workings.

Degenerative processes, even when sharply defined and dormant, are of little more help because such processes are always multiple. This objection still clings to Broca's demonstration of the sharply defined area of the brain responsible for motor speech. And it was the capricious effects of tumors and degenerative processes that led the famous Brown-Séquard so far astray in denying cerebral localization. How, he insisted, could such results be explained except by assuming that the brain worked as a whole?

The results of animal experimentation are of little value in determining cerebral functions and their localization because the advent in

human beings of the higher intellectual faculties, including the speech mechanisms, has brought about an entirely different set-up of the tracts in the central nervous system, particularly in their transfer, in part or in whole, to the cerebral hemispheres.

It is only necessary to mention the well known cerebral extirpations of Goltz's dogs to appreciate the dangers of attempting to transfer the results of canine experiments to the human brain.

The only accurate and safe data concerning most cerebral functions can come from extirpations of parts of the human brain. From accurately defined and well performed removals of this type the functional results, if positive, must be regarded as specific and, if negative, must exclude the part of the brain concerned from participation in the functions tested. Nor can Broadbent's old theory that the corresponding part of the opposite hemisphere assumes these functions be given even remote consideration. The arm, leg and visual areas receive no such relief, and losses of function due to injuries of the left hemisphere are not aided in the least by any participation of the right hemisphere. Before drawing conclusions of the positive type from local excisions of brain tissue it is necessary to be sure that an artery that supplies a distant part of the brain has not been included. It is clear that one could remove a small region of brain and include a middle cerebral artery, or one of its larger branches, and draw entirely erroneous conclusions from the disturbed functions. Then, too, a small zone of brain contiguous to the area removed in all probabillty will subsequently be destroyed by the operative trauma and will add somewhat to the total volume of tissue removed.

From the following three cases the physiological results following extirpation of the entire right cerebral hemisphere, *i.e.*, external to the basal ganglia, have been studied. One of these patients lived two years and two months, and the other six months.

*Case I.* R. F., a preacher, aged 32, was referred by Dr. John Booth of Rochester, N. Y., April 13, 1923. At the time of his admission to the Johns Hopkins Hospital he was in a state of semicoma; pulse 48; respirations 12 to 13, and irregular depth. He voided involuntarily in bed. Stimulation of the supra-orbital nerve produced movements of both arms and legs. The reflexes were normal. There was a suggestive but not definite papilloedema. The margins of the discs were hazy but the veins were neither full nor tortuous. As he had myopia of high grade,

it was not certain whether these changes were due to this local condition or to intracranial pressure.

From a fellow clergyman and friend who accompanied him it was learned that the patient had been a very brilliant student; in fact, he had been an honor man at the University of Virginia. He had always worked hard and was deeply interested in his studies. He was always eccentric and egotistical and was regarded as a queer person. He was seclusive, shunned society and took no interest in social matters. His friend had not seen him for a number of years until the previous summer. At this time he noticed a pronounced change. The patient talked continuously about sexual matters and was wont to stress this subject in his sermons. He harried his congregation a great deal and gradually they ceased attendance. He then became very nervous and agitated and complained bitterly of their unfairness. About this time he began to complain of headaches, principally in the right temporal region. There was a drawl in his speech but no aphasia. He had been more or less depressed for several months, probably because of the loss of attendance at his church. Three weeks before admission he had what was called a nervous breakdown, began to talk queerly and mumble to himself, and at other times would be depressed and unresponsive. But again there would be a flow of wit. Three months before he came to the hospital, he had stolen a communion set, but when the source of the theft was discovered he had maintained that it was his own property.

*Ventricular estimation* was performed April 13, 1923. The right ventricle could not be reached. The left was easily tapped and 25 cc. of fluid escaped under some pressure. From these findings a right-sided cerebral tumor was diagnosed.

*Operation April 13, 1923.* A fairly large bone flap was turned down on the right side. A subcortical tumor was found involving the frontal, parietal and temporal lobes. The tumor was clearly inoperable. The intracranial pressure was so great that it was necessary to remove the entire bone flap and in addition take away with the rongeur much of the remaining bone in the temporal region. The wound was then closed.

*Post-operative course.* Recovery was uneventful. The patient quickly regained consciousness. Four days after the operation a left hemiplegia developed progressively but quite rapidly. It was soon complete. There was a tremendous hernia at the site of decompression. Following the relief of pressure by the large decompression the patient gradually became clearer mentally. At first he wrote short notes to express what he wanted to say, then he began to talk but at times his speech was thick. He frequently joked and confabulated. He was fairly well oriented but had difficulty in maintaining intellectual contact. Occasionally he would refuse food. However, during the two weeks before the cerebral extirpation he had come to a high mental level and was in full grasp of his surroundings. He recognized old acquaintances even by their voices. He began to plan for the future and his confabulations became rarer and practically ceased. The patient and his relatives were very insistent that the tumor be removed even though they realized that the hemiplegia which was now complete would be permanent. Accordingly, at their request, the operation was undertaken.

*Second operation June 4, 1923* (seven weeks after the exposure of the tumor and decompression). The right cerebral hemisphere was subtotally resected, an area of occipital lobe remaining. The tumor had now reached the surface of the brain in the parietal and frontal regions. Two small cysts opened spontaneously. The anterior, middle and posterior cerebral arteries were separately clipped and divided. The tension in the brain was much diminished by the exclusion of the arterial blood. The veins passing between the hemisphere and the longitudinal sinus were then doubly clipped and divided as they crossed in the subdural space.

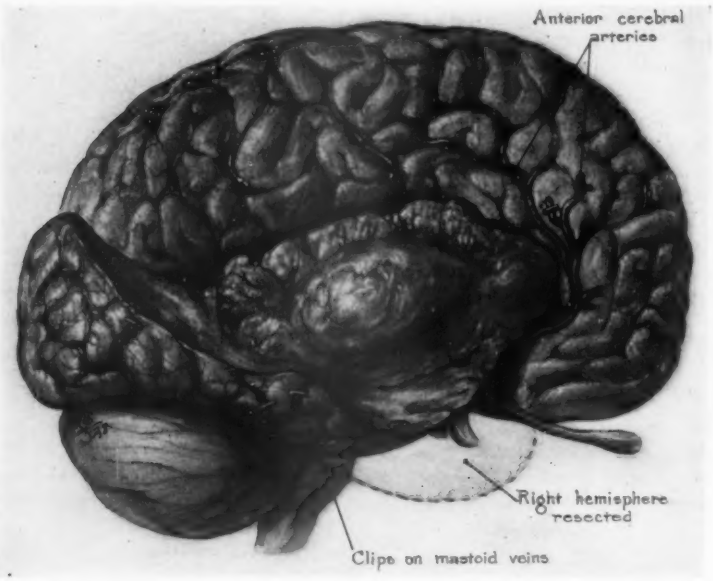


FIG. 1. DRAWING SHOWING EXTENT OF SUBTOTAL RESECTION OF HEMISPHERE IN CASE I

The hemisphere was separated from the falx. The corpus callosum was exposed and a lateral incision just above it opened the body of the lateral ventricle. The frontal, parietal and temporal lobes were removed, only a small portion of the occipital pole remaining (Fig. 1). There was everywhere so much tumor tissue that the brain ruptured in several places, exposing the growth. The total amount of extirpated brain tissue was 250 grams. In addition, there was the content of several cysts which were evacuated during the extirpation. It required 260 cc. of fluid to fill the cranial defect, and since there was a huge hernia before operation,

it is clear that the actual volume of tumor and brain removed was much greater than these figures would indicate. The basal ganglia were left intact (fig. 2). No tumor could be seen remaining in the hemisphere but the new growth had attached itself to the dura of the middle fossa. This portion was removed as thoroughly as possible by excising the dura.

*Postoperative course.* Recovery was uneventful. The right third nerve had evidently been traumatized during the operation, for ptosis and external squint were present immediately after it. This palsy gradually disappeared. Imme-

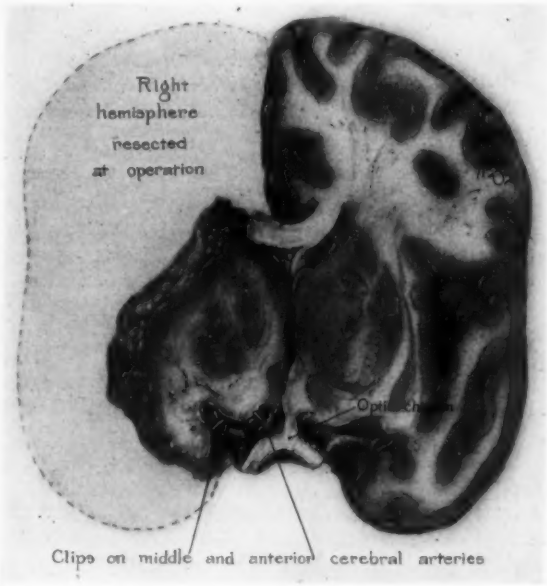


FIG. 2. DRAWING OF CORONAL SECTION OF BRAIN AFTER TOTAL REMOVAL OF THE RIGHT CEREBRAL HEMISPHERE ABOVE THE BASAL GANGLIA

diately following the operation his mental state was essentially the same as before the cerebral excision.

He was at all times perfectly oriented as to time, place and person. He was quite quick and accurate in repartee. On June 27, 1923, three days after the removal of the hemisphere, the following statement was recorded: "That's the sickest day I had since I have been here. I have headache and my stomach aches and my heel is sore. But I ought not to complain there are others who are

sick too. If you will give me an enema and get rid of this stuff in my stomach I will be better."

*June 9, 1923.* "How are you this morning?" "Better doctor."

"Any pain?" "In my head, heel, stomach, shoulder. I got enough to keep me busy."

"Date?" "9th of June, 1923."

"Who am I? "Dr. D."

"Who is your surgeon?" "Dr. D."

"I am Dr. H., did you see me before?" "Yes, several times."

"Which day of the week is this?" "Friday, unlucky day."

"Why unlucky? Everybody says Friday is an unlucky day. I don't know why. Old folk-lore or from the old witchcraft days, perhaps."

"How was the sherry wine you got yesterday?" "That was fine."

On July 13, 1923, five weeks after extirpation of the hemisphere he dictated the following letter:

"Dear Father and Mother:

Mr. Mason read your last letter to me, and it gave me much joy and comfort. There isn't much to write about that is new. I am perfectly well as far as my head is concerned, the only thing that is holding me back is my paralyzed leg and arm. I asked the doctor the other day when I could go home and he couldn't give me any definite answer, of course, nor can I imagine when it will be. It will be within a month I am sure. I told the doctor that I wanted to eat Thanksgiving dinner with you all at home, and he said that he thought that this could be possible. Everyone is very kind to me here. I have made many dear friends. My love and God's blessing upon all the dear ones at home. I think of you continually every day.

Your loving son,

Roy."

"P.S. The nurses in the offices have bought me several little things for which I am indebted. Please send me five one dollar bills again. This will probably be all the money I shall need.

Roy."

Following is a list of puns with which he entertained his friends both before and after the time his hemisphere was excised:

Why does a duck go under water? For diverse reasons.

Why does he come up again? For sundry purposes.

Why is the heat around the furnace like a circus? It is intense.

Why does a crow? Caws.

If you saw a Ford automobile driving down the street, and another passing it, what time of day would be represented by the scene? Ten after ten.

Why is it that next year all Fords have to be painted red? Because it is the fire law that all gasoline cans must be painted red.

Why didn't Eve have the measles? She had Adam.

After man came woman and she has been after him ever since.

I am getting worried about my hand. I want to play music for you in the hospital, and need the use of this hand for music. I play the guitar. One of the boys out there made me laugh. He said he was a musician. I said, "What music do you play?" and he said, "The victrola."

The extirpation of the hemisphere had no effect upon the facility and accuracy with which they were rattled off. Although showing no high mental level, they at least indicated a retentive memory.

On July 24, 1923, at the time of discharge, the following observations are recorded by Dr. Ford:

*Cranial nerves.* II. Complete homonymous hemianopsia for form and color.

V. Muscles of mastication contract strongly on the left (the paralyzed) side. Sensation is not grossly diminished in the face. Point of a pin recognized. Cotton well felt. Corneal reflex equal on both sides.

VII. The left side of the mouth does not move with voluntary efforts. When the patient smiles there is some slight movement. Eyelid closes tightly on the left. The forehead wrinkles on the left, though less strongly than the right.

VIII. Patient hears watch equally well on both sides.

XI. Sternomastoids move equally on the two sides. The left shoulder can be elevated.

XII. Tongue protrudes in the midline.

*Motor and sensory changes.* There is complete paralysis of the left arm. The left leg can be flexed at the knee but cannot be extended. No movement of the toes or ankles. The muscles are all flabby. There is no spasticity. There is loss of all cutaneous sensations on the left side, except as noted in the face. Vibration of the tuning-fork is perceived on the left but not so strongly as on the right. There is complete loss of sense of position and of passive movements. Movements of the joints and compression of the muscles cause intense pain on the left. The tendon reflexes are greatly increased on the left. There is an ankle clonus, and active Hoffmann on the left. Abdominal reflexes equal. One month ago the abdominal reflex was absent on the left. Plantar stimulation on the left causes flexion of the leg but no movement of the toes. The patient retains complete sphincter control.

The patient left the hospital July 24, 1923. On June 25, 1925, I visited him at an institution maintained by the church for invalids. His mental faculties appeared to be quite normal and had so impressed his friends. He was interested in the radio, conducted vesper services on Sundays and read scripture lessons. His articulation and memory were good. He enjoyed the radio and listened with the greatest interest and late into the night to the proceedings of the Democratic National Convention which was in session in New York City during the summer. He also read the newspapers. The following month he began to become irritable and signs of weakness of the other side developed. It was evident that the tumor

was recurring. He died August 16, 1925—two years and two months after extirpation of the cerebral hemisphere.

*Case II.* Mrs. A. S., aged 24, entered the Johns Hopkins Hospital October 13, 1927. Complaint: Weakness of the left side of the body. Family and past histories, negative. Five weeks ago numbness of the left arm, particularly of the hand, was first observed; ten days later the weakness had extended into the arm. A few days afterward left facial weakness was evident. The arm became progressively weaker. Two weeks ago, or three weeks after the first symptom, the left foot began to drag and it too has become progressively worse. There have been no headaches, no mental changes or other disturbances.

*Physical and neurological examinations.* A well nourished, well developed woman, intelligent and alert. The eyegrounds are entirely negative. There is a partial paralysis of the left hand and wrist. The biceps and triceps are weak, but not entirely paralyzed. The left leg is partially paralyzed; she can drag it in walking but it is of little service. There is perhaps slight diminution of the left corneal reflex and slight loss of sensation over the left hand and forearm, but no demonstrable changes in sensation elsewhere on the left side are noted. The reflexes in the left arm are markedly exaggerated; and the arm is spastic. The knee-kicks are greatly increased on the left. The Babinski is positive on the left—negative on the right. There is no ankle-clonus. X-ray of the head negative. Blood pressure 125/80.

*Diagnosis.* The gradually progressive weakness of the entire left side could scarcely be due to any lesion except a tumor, and because of the rapid progress it was thought to be around the internal capsule. However, an air injection was considered in order to eliminate possible lesions of other type, particularly since removal of the hemisphere was considered in treatment. The absence of headache and papilloedema suggested a small tumor that was producing only local disturbances and not those of intracranial pressure.

*Ventriculography.* The right lateral ventricle could not be reached; the left ventricle was small. There was no evidence of intracranial pressure, the fluid dripping from the needle. About 15 cc. of air were injected. The air failed to pass into the right ventricle. The third ventricle was definitely though only slightly oblique. There appeared to be no dislocation of the anterior horn of the left lateral ventricle. These findings made it certain that patient had a small tumor in the right cerebral hemisphere.

*Operation, October 25, 1927,* three days after the air injection. Under ether anesthesia a bone flap was turned down over the right hemisphere. The dura was under no evident pressure. The surface of the brain at first appeared to be normal, but on closer inspection a slight change in the convolutions of the face and arm center in both the prerolandic and postrolandic areas was seen. The whole area involved was roughly circular and about 2.5 cm. in diameter. To make absolutely certain of the character of the lesion a nasal dilator was passed through this area

and at a depth of 4 cm. a reddish-brown, semigelatinous tumor was encountered. The nasal dilator was then withdrawn. It was evident that the only chance of successful extirpation of this tumor, which was clearly of the infiltrating type, was by an extensive resection. One could perhaps have resected the territory immediately surrounding the tumor, but this would have produced precisely the same disturbances as resection of the hemisphere, and the chances of a successful extirpation would have been very much reduced. An extension of the bone-flap was then made anteriorly. The frontal lobe was elevated, the carotid artery was doubly clipped alongside the optic nerve, and immediately following this the anterior cerebral, middle cerebral and the posterior communicating arteries were doubly clipped and divided. At once the volume of the cerebral hemisphere was markedly reduced. The veins passing to the mesial border of the hemisphere were then ligated with silk sutures just before they left the brain tissue to cross the longitudinal sinus. It was easier and safer to ligate the vessels in the brain substance than in the free subdural space, *i.e.*, between the hemispheres and sinuses. An incision was then made through the cortex from the frontal to the occipital region, leaving a small, triangular rim of brain substance lining the entire longitudinal sinus and carrying the venous stubs. The hemisphere was then separated from the falx. The corpus callosum was brought into full view. A lateral incision in the mesial surface of the hemisphere, just above the corpus callosum, brought us into the lateral ventricle. The hemisphere was then elevated with the finger in the lateral ventricle, and excised at the basal ganglia. To facilitate the extirpation the frontal lobe was resected separately, the remainder of the hemisphere, including the temporal, parietal and occipital lobes, being removed in a single mass. The lateral ventricle was now wide open. The choroid plexus and the body of the ventricle were in full view. In extirpating the mass the posterior cerebral artery was encountered and ligated. There was very little bleeding. Inspection of the mass failed to show any sign of tumor on the cut surface. The tumor was disclosed only after a later sectioning of the mass of brain tissue (fig. 3). The weight of the brain tissue removed was 375 grams. The dura was closed tightly, the bone-flap wired in place, and the muscle, galea and skin were closed with interrupted sutures of silk.

*Postoperative course.* When the patient left the operating room her pulse was 95, respirations 32, temperature 101.4°F. In the afternoon she talked and moved her right arm and leg. During the evening and night she talked quite readily and apparently normally. There was then perhaps slight spasticity of the left arm and leg and the Babinski was suggestive. At nine o'clock her pulse changed, was difficult to count but was running around 130 to 140, and she was quite restless. Temperature 102.4°, respirations 36. For the next two days her condition remained very much the same except that she responded poorly. She was in fact difficult to arouse. Respirations remained rapid, pulse around 100, temperature 100 to 102°. In the interim she had had several ventricular punctures but with no marked effect. At no time was there bleeding within the

great cerebral cavity, the fluid always returning clear but under some pressure. On the third day a flanged needle was inserted into the frontal region to provide continuous drainage; it was left in place for two days. Her condition seemed to improve somewhat though I question whether this procedure produced the change. At any rate it unquestionably was the source of an infection which soon developed,

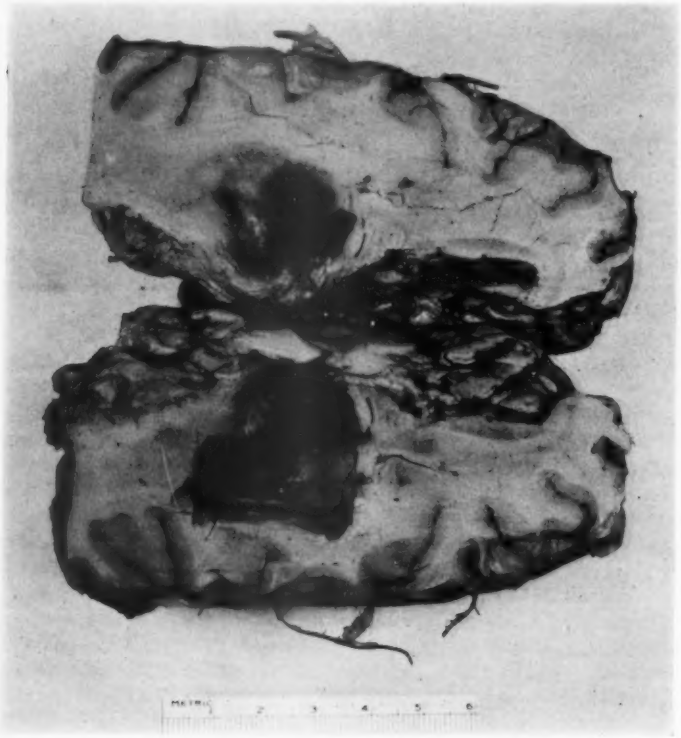

FIG. 3. SECTION OF BRAIN WITH DEEP SUBCORTICAL TUMOR (CASE II)

and which, though of an indolent type, nevertheless was ultimately responsible for her death. In the course of the next two weeks the infection became highly purulent and required drainage through an incision and removal of the bone flap. The huge cerebral cavity filled with pus although the foramen of Monro became sealed and prevented meningitis. Her temperature gradually returned to normal.

She left the hospital two months after her operation. The infection could never be eradicated nor satisfactorily handled, and she died six months after operation.

*Mentality.* The extensive infection is a complication which I feel must be taken into account when testing her mentality. Her brother, who is a doctor, thought that for several weeks after the operation her mind was perfectly normal. However, there were little disturbances, as evidenced by the following note by Dr. Diethelm on December 19, 1927, seven weeks after the operation: "I saw Mrs. S. on two occasions—December 15 and 17. During the first interview she was irritable and did not want to talk at all. She had many complaints, physical complaints as well as about the nurses and the hospital, all said in a very peevish manner. Her stream of talk was always coherent. She was not depressed and her sensorium seemed to be more or less clear. She was oriented as to place, time, situation and person, but she did not remember events of the last twenty-four hours and gave an inaccurate account of her past life Her judgment was rather poor. She did not seem to understand her treatment and showed a very poor understanding of her own peevishness and also of her poor memory for recent events.

"Last Saturday (17th) the patient was quite different. She was more alert, talked freely and joked, but the jokes were about trivial things and in a silly way. She was less irritable but still impatient. She smiled and felt more or less at ease. She still has difficulties in understanding orders, *i.e.*, she wants to get up although she knows that she cannot do it. These reactions are probably more the determination of a stubborn personality. Her sensorium is perfectly clear and her memory intact for recent and remote events as far as I was able to test it. The mistakes which she made were due more to fatigue and to a lack of being able to concentrate on certain topics for any length of time.

"I explain the difference in the two examinations by a certain cloudiness which was present the first time and which I would explain with her present organic condition. The second examination argued against an organic deficit."

In estimating her mentality it is necessary to state that she had had very little education, only going through the primary grades.

On the 20th of December, 1927 (two months after operation) the following mathematical tests were made:

9 × 7—Answered 63 promptly.

12 × 12—Answered 144 promptly.

When asked to divide 144 by 12 said "I cannot do that without a pencil."

25/5—Answered 5 fairly promptly.

30/3—Answered 10 promptly.

When asked to subtract 3 from 30, said "What are you, a teacher or a doctor?" and then said "27" promptly.

Asked to add 30 and 3—Answered promptly.

She reads quickly and correctly. Can spell various names that are suggested and does so promptly without error. She learns words that she has never heard

before and remembers them on subsequent days. She writes correctly and makes correct punctuations. She is facetious, suspicious and easily bored, but her brother says that she has always been so. She coöperates only when she desires to do so.

*Neurological tests for function*

*Cranial nerves.* I. Her sense of smell is very keen—she detects various odors promptly.

II. There is complete left homonymous hemianopsia for forms and colors.

III, IV, VI. All of the extraocular movements are normally performed without restriction. There is no nystagmus.

V. There is marked preservation of sensation over the left side of the face and corresponding exactly with the trigeminal domain. Light touch is not perceived, but when touch is slightly intensified, as by rubbing loose cotton over the face, it is accurately recognized and located. The point of a pin is registered as a painful stimulus. Sharp and dull are easily differentiated but both are considerably less acute than on the right side of the face. Heat and cold are accurately defined, though here again a somewhat greater degree of temperature is required than on the other side. The masseter muscles contract on both sides, but with somewhat less force on the left. However, the jaw is not deflected from the midline when the mouth opens. The corneal reflex is very acute and essentially the same on both sides. It will be observed that a diminution of the corneal reflex was observed in the preoperative examination.

VII. There is definite asymmetry of the face, greater contraction being, of course, toward the right, but much movement is retained. The forehead wrinkles on both sides about equally well. There is a deep nasolabial groove on the left side and the eyelids close together and completely, and almost with equal force. There is only a little less wrinkling of the corner of the eyes on forceful closing of the lids.

Taste tested on the 20th of December, 1927—two months after operation:

| | *Right* | *Left* |
|---|---|---|
| Sugar | Promptly | 0(?) |
| Salt | Promptly | 0(?) |
| Acid | Promptly | Promptly |
| Bitter | Promptly | Five seconds |

There is, therefore, definitely some taste. Unfortunately examination for taste was not made before operation. It cannot, therefore, be known whether there has actually been a postoperative loss of taste, or whether this might perhaps be the normal for this side.

VIII. Patient's hearing has been perfectly normal since the operation. There has been not the slightest sign of unilateral deafness and there has been no tinnitus. An audiometer test was made by Dr. Bunch on February 27, 1928, or four months after the operation. The hearing was essentially the same on both sides (fig. 4).

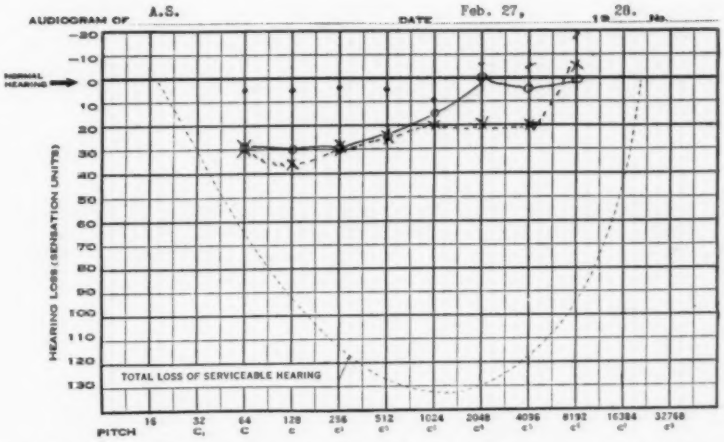


FIG. 4. AUDIOGRAM FROM PATIENT (CASE II) WHOSE HEMISPHERE HAD BEEN REMOVED FOUR MONTHS PREVIOUSLY

FIG. 5. PHOTOGRAPH OF HEMISPHERE REMOVED FROM PATIENT (CASE III)

XI. The left sternomastoid and trapezius muscles function but are weaker than on the other side.

XII. Tongue is protruded in the midline.

*Motor and sensory changes in arm and leg.* No movement whatever is possible in the left arm. There is slight movement in the muscles of the foot but they are

very feeble and she cannot bend the toes or elevate the foot from the bed. No movement is possible at the knee or thigh. Cutaneous sensation is abolished over the entire left side except over the trigeminal domain, as described above. However, a deep sensation of a certain kind is present on the whole left side. When the muscles of the leg or arm are squeezed, the patient complains of severe pain and, moreover, is able to localize with fair accuracy the area that is squeezed.

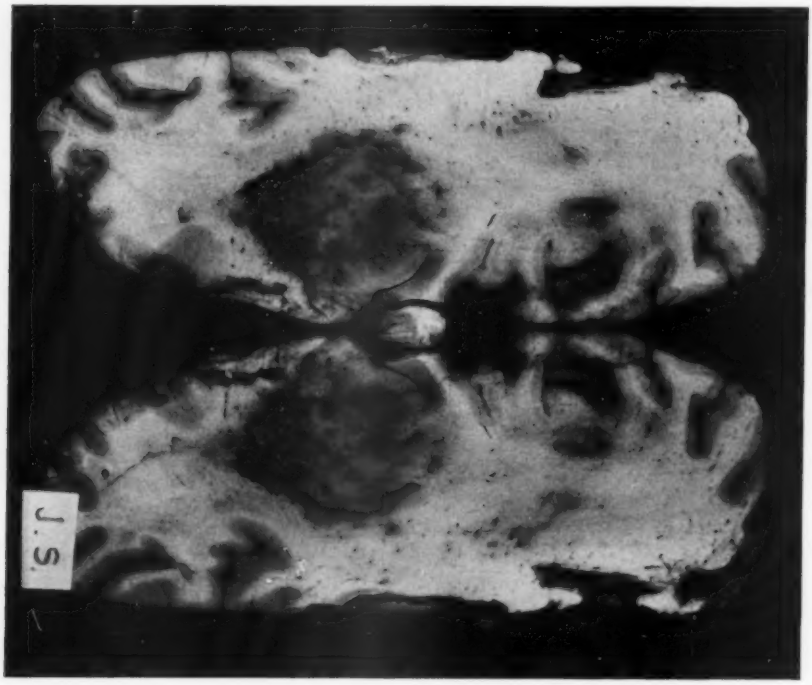


FIG. 6. SECTION OF HEMISPHERE SHOWING TUMOR (CASE III)

When the toes are manipulated, she can identify the one moved but cannot tell whether it is elevated or lowered. When the sole of the foot is scratched, the whole left leg draws up. She can tell when the leg is elevated or lowered. (Deep sensation is unchanged on the right side.) There is also severe pain on manipulation of all the joints on the left side. There is no spasticity of the left leg. Although the left hand tends to a claw formation, it is quite easy to open the fingers. There is no contracture of the forearm or the upper arm, nor is there contracture

of the leg. Except for the slight claw formation of the hand one would consider the leg and hand to be in a flaccid state. There is no resistance to passive manipulation of the arm at the elbow or the leg at the knee. There are ankle and patellar clonus on the left. The biceps and knee-kicks on the left are slightly greater than on the right. There is at times an equivocal Babinski on the left; at other times it is negative. Superficial reflexes on the left side of the body are absent. Oppenheim and Gordon tests on the left are positive. Abdominal reflexes are active on the right, absent on the left. Vibration sense is lost over the entire left arm and leg.

*Case III.* The following is a record of the conversation—necessarily limited—beginning twenty-four hours after extirpation of a right cerebral hemisphere and contained tumor (figs. 5 and 6) (total weight 584 grams) in a colored man, and continued at intervals during two days, after which meningitis ensued and caused his death ten days later. At the end of the reported conversation he began to become incoherent and irrational from the effects of the high fever. It is, I think, evident that immediately after the operation and before complications developed his mind functioned quite normally.

Operation concluded March 16, 1927, 12 noon.

*March 17, 1927:*

2:00 p.m. "My left wrist pains." Holding wrist with right hand.

2:10 p.m. *Q.* "Can you straighten left leg?" No answer, but pushed it down straight by using right leg.

2:30 p.m. *Q.* "Can you raise your knees while I put this pillow under?" Raised right leg.

*Q.* "Does your wrist still hurt?"

*A.* "Yes mam—right here"—pointing to wrist.

3:00 p.m. *Q.* "Are you trying to sleep?"

*A.* "Yes, I'm trying, but its pretty hard."

*Q.* "When are you going to stop hiccoughing?"

*A.* "I don't know, but I'd like to."

Asked by orderly if he needed attention, answered "No."

3:20 p.m. *Q.* "Does your side hurt?"

*A.* "No miss."

*Q.* "Not at all?"

*A.* "Just a little."

3:45 p.m. *Q.* "Perhaps if you talk a bit the hiccoughing will stop."

*A.* "It might."

*Q.* "Did you work before coming into the hospital?"

*A.* "I worked until the 15th of December, then I had to quit, I couldn't work any longer and I came into the hospital."

*Q.* "Is that when you had your first operation?"

*A.* "No, I had that in 1924."
*Q.* "What work were you doing?"
*A.* "I worked for Baltimore Steel Company."

5:00 p.m. Answers all questions promptly, no hesitation, apparently no lack of memory. Speech not impaired at all. Voided involuntarily. When asked if he knew when he must void, answered "Yes," but offered no answer when asked why he didn't ask for some one to take care of him.

6:00 p.m. Asked during dressing if head hurt more than before puncture was started.

*A.* "Yes, it hurts more now."
*Q.* "Would you like to have some milk?"
*A.* "Yes, I would."

7:00 p.m. *Q.* "Did you enjoy the milk?"
*A.* "Yes, it was very good."

9:00 p.m. "I want the orderly, please."

9:30 p.m. *Q.* "Does the light hurt your eyes?"
*A.* "No, miss."
*Q.* "Does your chest hurt?"
*A.* "It's not so sore."

10:00 p.m. *Q.* "Does your right hand hurt?"
*A.* "No, just feels numb."

10:45 p.m. *Q.* "Do you know where you are?"
*A.* "Yes sir."
*Q.* "Where?"
*A.* "In Johns Hopkins Hospital."
*Q.* "Do you know who I am?"
*A.* "Yes sir."
*Q.* "Who?"
*A.* "Let's see. Who are you?" After a pause.
*Q.* "Who did you come here to see?"
*A.* "Dr. Dandy."

11:45 p.m. *Q.* "What month is this?"
*A.* "March."
*Q.* "What day of the month?"
*A.* "Let's see" answered after a longer pause than usual.
*Q.* "How do you feel?"
*A.* "I feel fairly good."

*March 18, 1927:*

1:45 a.m. (48 hours after operation) *Q.* "Would you like some orange juice?"
*A.* "Yes Miss."

4:00 a.m. *Q.* "Do you want some more water?"
*A.* "Yes Ma'm."
6:00 a.m. *Q.* "How do you feel?"
*A.* "All right."
8:00 a.m. *Q.* "How do you feel this morning?"
*A.* "I feel right good, but I've got a pretty heavy fever." Pulling at clamps on infusion.
9:30 a.m. *Q.* "What do you want, Raymond?"
*A.* "I don't want anything."
*Q.* "Can you see that?"
*A.* "Yes Ma'm." Pulling at dressing.
10:00 a.m. *Q.* "Why are you doing that?"
*A.* "It feels like its coming off"
10:30 a.m. Playing with clamp on infusion.
*Q.* "What are you doing with that?"
*A.* "I'm going to play some music."
*Q.* "How?"
*A.* "Just turn it and it plays."
*Q.* "What is it, a Victrola?"
10:45 a.m. *A.* "No'm, its a radio."
*Q.* "How do you feel now?"
*A.* "Oh, I can't say I feel so good and I can't say I feel so bad, just about the same, I guess."
12 noon. Visited by head nurse of ward; Recognized her immediately. Told her he felt quite well and would enjoy coming back to ward.
12:20 p.m. Seen by Dr. Dandy.
*Q.* "Where are you?"
*A.* "At Walter Young's."
*Q.* "Who did you come to see here?"
*A.* "Dr. Dandy"—slight hesitation.
*Q.* "Now can you tell me where you are?"
*A.* "Johns Hopkins Hospital."
*Q.* "What month is it?"
*A.* "March."
*Q.* "What year?"
*A.* "1927."
12:30 p.m. Cold sponge (begun to reduce temperature).
"It's too cold to take a bath with that water, it's almost like ice."
Asked for orderly. Voided voluntarily.
3:30 p.m. Began talking of his own accord.
"They could get a lot of things around here to build."

*Q.* "What things?"
*A.* "Grass and things."
*Q.* "What is this place?"
*A.* "Johns Hopkins Hospital."
*Q.* "What would they use the grass for?"
*A.* "To build a nest for the young ones."
*Q.* "Who would?"
*A.* "The mice."
*Q.* "I didn't know that mice used grass for nests."
*A.* "Yes Ma'm, and feathers and cord and things."
*Q.* "What made you think of mice?"
*A.* "I don't know, I just thought of them."

5:15 p.m. *Q.* (By patient) "Is there some ether in that?". Referring to alcohol.
*A.* (By nurse) "No, does it smell like ether?"
*A.* (By patient) "Seems like everything smells like ether now."

6:10 p.m. $3.00 mentioned without any provocation.
*Q.* "What do you want $3.00 for?"
*A.* "To go to Cambridge."
*Q.* "Why do you want to go there?"
*A.* "My wife wants to go."
*Q.* "Why?"
*A.* "Because her mother's there."
*Q.* "Does it take $3.00 to go there?"
*A.* "No, $1.65."
*Q.* "Don't you have that much?"
*A.* "Oh, yes'm."
*Q.* "If it's only $1.65, why do you need $3.00?"
*A.* "You see my wife's got to go and I've got to go."

## SUMMARY AND CONCLUSIONS

The presentation of these three cases with extirpation of such vast areas of brain tissue without the disclosure of any resulting defect in mental functioning is most disappointing. It is still difficult to believe that some functions of the mind are not stored or at least are not activated there. Needless to say one would experience much greater elation in finding some well defined facts of positive type than in making the sweeping negative deduction that is suggested here. I am still not willing to say that the mentality of the patients was normal; but rather that abnormalities have not been disclosed. And it need scarcely be added that I have sought evidence of positive func-

tions by referring these patients to the best available talent. I realize too that the best proof of a normal mind is the ability to carry on in the competitive world, and this opportunity was denied these unfortunates because of the hemiplegia. Then, too, little peculiarities of mental origin, such as those in the famous crow-bar case, may escape mental tests but be obvious to those who are thrown in frequent intimate contact. But such defects, if any, escaped us during the postoperative period and subsequently did not become apparent to the friends of the first patient who were associated with him in the sanitarium for over a year and a half. It is realized too that the opinion (in Case II) of a brother that his sister showed no mental abnormalities may be accepted with reservations.

It is interesting that the first patient had pronounced and progressive mental changes before his operation. These gradually cleared after the relief of intracranial pressure and remained absent after excision of the cerebral hemisphere—a splendid example of the referred effects of the tumor to that part of the brain.

Both patients were always perfectly oriented as to time, place and person. Their memory for immediate and remote events was unimpaired. They could read, write and compute without error. Moreover, the first patient (the infection reduced the period of activity in the second case) was always quick, alert and keen, as evidenced in his style of humor, but he was also interested in serious conversation, in reading and in following the world's events. His originally defective and now additionally impaired vision (hemianopsia), however, curtailed extended reading. His concentration was, I think, quite normal. Both patients were always coherent; at no time were there abnormal fears, delusions, hallucinations, confabulations, expansive ideas or obsessions. Neither was there undue melancholy nor euphoria. Both seemed emotionally quite stable, although the second patient was irritable and peevish at times. Both were normally concerned about the loss of power in the left side but knew that the handicap must be accepted and learned to do so. The habits of both were normal so far as one could judge. The habits of both were always cleanly. There was no tendency to coprolalia.

*Other neurological functions.* One of the most interesting findings is the preservation of function in the domain of the cranial nerves, *i.e.*,

evidence of autonomy of these nerves. *Hemianopsia* is, of course, complete. *Smell* is unaffected. *Taste* is preserved at least in part; the evidence is not sufficient to say whether or not it is modified.

*Hearing* is not altered. In an earlier paper this finding was used as proof of the absence of an acoustic center in the right temporal lobe as has long been hypothecated. And as neither patient was ever dizzy, it is fair to assume that no essential vestibular connections are present. Unfortunately a Bárány test was not made.

None of the extraocular movements were altered or impaired in the slightest, nor was there nystagmus at any time in either case.

Of the greatest interest was the preservation of function in the trigeminal and facial nerves, both of which are known to have cortical representation. In one case there was a very definite but slight diminution of all forms of sensation, corresponding exactly with the trigeminal domain. In the other case it was noted that there was no sign of diminished sensation. Over the remainder of the left side of the body cutaneous sensation was abolished. The motor function of the trigeminal nerve, as evidenced by the degree of contraction of the masseter, temporal and pterygoid muscles, was possibly slightly but certainly not much depreciated. The corneal reflex was equally active on both sides in both patients.

The motor power of the facial nerve was definitely diminished but was nevertheless remarkably well preserved. Both patients could close the eyes well and move the corner of the mouth though the nasolabial groove was much shallower than on the normal side. Apparently the degree of preservation and loss of this function varies in different individuals, for in other extirpations (with shorter survival periods) there was marked difference in the degrees of facial function.

The motor power in nerves X, XI and XII is also little, if at all affected. The tongue protruded in the exact midline in both cases; and the sternomastoid and trapezius muscles appeared equally strong on the two sides. The absence of hoarseness and of difficulty in swallowing would also surely indicate preservation of the function of the vagus. Unfortunately the sensory domain of the glossopharyngeal nerve was not tested.

Another point of interest is the preservation of some (though very slight) movement in the leg of both cases. It was of no practical value

in either instance. The flaccidity of the extremities was most surprising. There were no contractures, such as one sees in the many clincial examples of hemiplegia. Indeed there was very little, if any, resistance to passive movements at any time of either the arm or leg. However, the deep reflexes—biceps and knee-kicks—were greatly increased on the left in one case and but slightly in the other. An ankle and a patellar clonus were present in both cases. A positive Babinski was not present in either case.

These findings are quite different from those obtained in dogs or cats, in which the removal of a hemisphere causes no disturbance of gait and no spasticity. The great rigidity from injury to the motor tracts in dogs and cats (decerebrate rigidity) is in evidence at the midbrain. In human beings the rigidity follows lesions in the cerebral cortex and subcortex and is entirely lost or essentially so at the outer border of the basal ganglia, below which control over motor function is lost. The slight preservation of motor power in the legs of our patients is doubtless evidence that a slight residue of function is mediated by lower centers, probably like that in the dog.

The preservation of sensation in the joints, the acute pain when the deep muscles are compressed demonstrates the existence of sensations that are mediated at a lower level than the cortex. Whether or not these sensations arise from sympathetic nerves (or in part at least) is not known. In one case (Case II) there was accurate recognition of the location of the muscles that were squeezed and the joints moved. Even the toes that were flexed or extended could be accurately identified although the direction of movement was not known. These observations were checked many times. On the other hand, it is noted in Case I that there was complete loss of sense of position and of passive movements. Vibratory sense is recorded as being absent in Case II and present in Case I.

The abdominal and corneal reflexes were unchanged in both cases.

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# TREATMENT OF MÉNIÈRE'S DISEASE BY SECTION OF ONLY THE VESTIBULAR PORTION OF THE ACOUSTIC NERVE

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Received for publication June 2, 1933

The cure of Ménière's disease by section of the auditory nerve intracranially is now established. Following this operative procedure, which has now been employed in thirty-five cases,[1] there have been no subsequent attack of dizziness, no loss of life and no disturbance of function, except in two of the early cases when the facial nerve was injured—a danger which is now scarcely possible. The only loss from the operation has been permanent deafness in one ear, but since there is always subtotal deafness at the time of operation, the actual loss caused by section of the eighth nerve has been of no practical concern. However, there are times when, from a number of irrelevant causes, the contralateral hearing is also diminished. In such instances preservation of hearing on the affected side, particularly if magnified by electrical instruments, might at the present or even at some future time be of important service. And again there are times when the actual loss of hearing in the affected ear—especially in the early stages of the disease—may be relatively slight.

After the cure of Ménière's disease had been established, there naturally suggested itself the possibility of a further refinement by which the remaining hearing on the defective side would be preserved Since the disturbing symptoms of Ménière's attacks are due to explosions of function in the vestibular component of the nerve, it is reasonable to expect that section of only the vestibular division of the nerve would cure the attacks, while hearing might be left intact. Since there is no gross demarcation between the auditory and vestibular

[1] Dandy, W. E.: Ménière's Disease; Diagnosis and Treatment. Report of Thirty Cases. *American Journal of Surgery*, 1933, xx, 693.

divisions of the acoustic nerve where it is attacked surgically, the exact limits of the vestibular branch can only be estimated. It was assumed that the vestibular division made up one-half of the volume of the nerve. But to be certain that all vestibular fibers were included it would even be advisable to divide some of the anterior fibers of the auditory division of the nerve. From experiences with the sensory

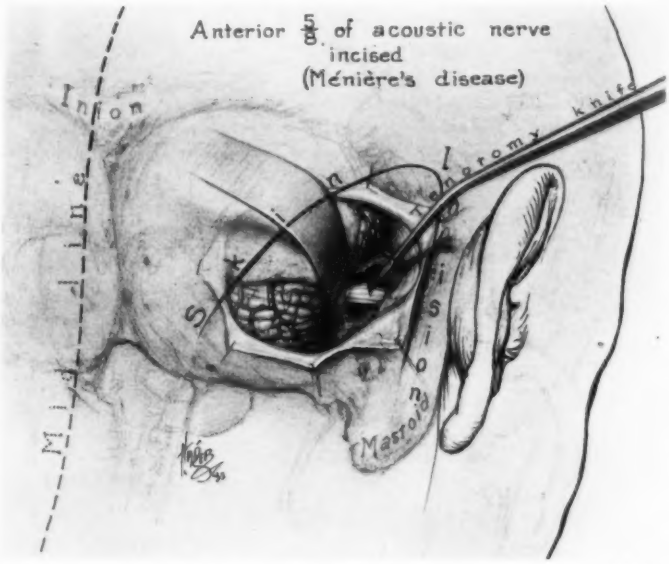


FIG. 1. DRAWING SHOWING OPERATIVE APPROACH AND MANNER OF DIVIDING THE VESTIBULAR BRANCH OF THE AUDITORY NERVE LEAVING THE ACOUSTIC DIVISION INTACT

root of the trigeminal nerve, and perhaps of the optic nerve also, there was reason to believe that loss of some auditory fibers might not be followed by reduction in hearing. The experiment at least seemed worthy of a trial and it succeeded.

## CASE REPORT

Male, age 51; some deafness in the right ear for twenty-six years; increased deafness in the past eight months. Humming in the right

ear six months. During this time there have been frequent attacks of dizziness, lasting one-half to one hour. They have averaged about two a week. During attacks there is sound like that of church bells ringing in the right ear. He is nauseated and vomits. Dizziness is worse when lying down and when the eyes are closed. During attacks objects turn clockwise and the patient staggers to the right. Between attacks he is free from all symptoms, except tinnitus, the intensity of which, however, is greatly reduced.

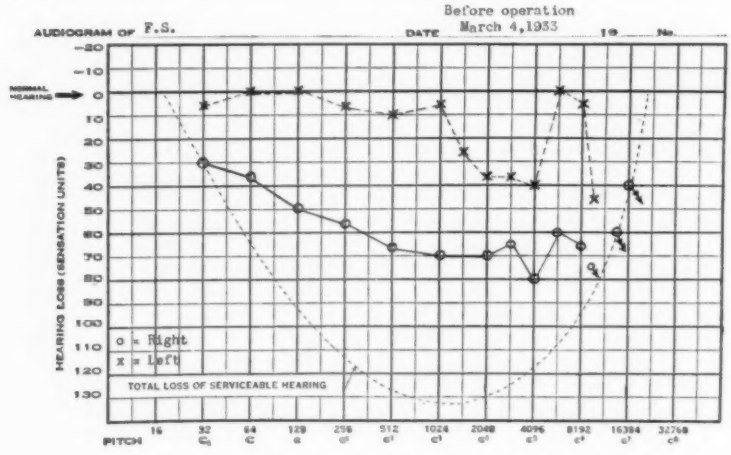


FIG. 2. AUDIOMETER CURVES BEFORE OPERATION

Exmination is negative except for the audiometer and vestibular reports. Vestibular (Bárány) test: Normal response to hot and cold on the left; reduced but fairly active response on the right.

*Audiometer test.* The audiometer curves are shown in figure 2. A marked loss of hearing in the good ear made it necessary to preserve the hearing in the defective side for possible future service.

*Operation, March 10, 1933.* Partial section of the eighth nerve was performed under avertin anesthesia. The nerve was cocainized before division. Approximately the anterior $\frac{5}{8}$ of the nerve in cross section was divided; the posterior $\frac{3}{8}$ of the nerve (the auditory part) was preserved (Fig. 1). Assuming that the eighth nerve is equally divided

(in cross section) between the auditory and vestibular divisions, the total vestibular branch should have been divided, and approximately an additional $\frac{1}{8}$ of the nerve, *i.e.*, about $\frac{1}{4}$ of the total volume of the acoustic branch, was added in order to be reassured that no vestibular fibers could be retained in the acoustic nerve.

The postoperative course was uneventful.

*Postoperative caloric test* (13 days after section of the nerve): Total loss of all reactions on the right; normal on the left.

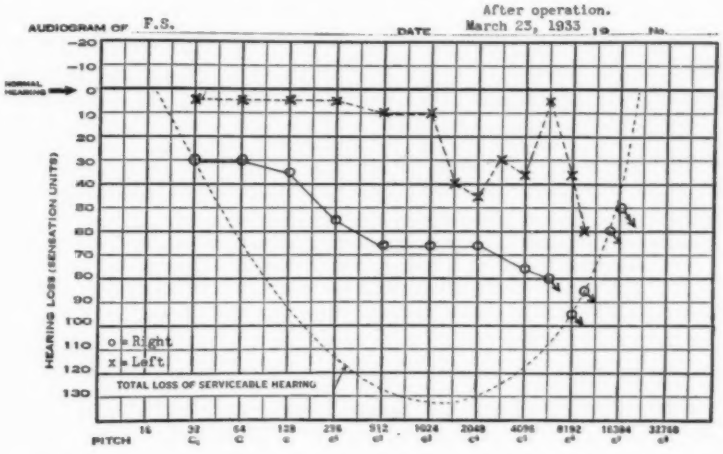


FIG. 3. AUDIOMETER CURVES THIRTEEN DAYS AFTER SECTION OF THE VESTIBULAR DIVISION OF THE NERVE

*Audiometer curve.* The only change from the preoperative audiometer test was a loss of the octave above 4096 (Fig. 3). Whether this slight change is actual or significant, I am not prepared to say.

The time (April 18, 1933—five weeks after operation) is as yet much too short to claim a permanent cure of the Ménière's syndrome by section of only the vestibular division of the auditory nerve, but the total absence of the caloric response indicates total absence of function in this division of the nerve and leads us to believe that a successful outcome, and with practically no loss of hearing, may be expected.

# TWO USEFUL STAINING METHODS FOR THE HUMAN HYPOPHYSIS

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Submitted for publication May 10, 1933

The two methods to be described have been found to stain differentially in the same section the eosinophil and the basophil cells of the human hypophysis removed at autopsy. They were arrived at after trial of many methods, the best of which are based on fresh animal or human operative material. The fixation permits the preparation of sections through the whole hypophysis, rather than from bits of tissue. The first, using fuchsin methyl-blue, is a modification of one of Bailey's (1) methods, with the substitution of aqueous methyl-blue for acid violet. The methyl-blue was found to have less decolorizing action on the fuchsin and with autopsy material a greater affinity for the basophil granules. We were saved from error in supposing the second method, the eosin-methyl-blue stain of Mann (2), to be an original application, by finding it referred to by Romeis (3) and by Collin (4). The differentiation of the present method has been found preferable.

*Fixation.* The hypophysis is fixed for 24 hours in Zenker-formol, or more correctly, Helly's fluid, that is, 90 cc. of Zenker's fluid without acetic acid, plus 10 cc. of 40 per cent formalin, the mixture being made immediately before use. The hypophysis should be cut into two or better into three blocks. Paraffin sections are made; these are treated to remove the paraffin, then passed through graded alcohols, and the mercury precipitate removed in the usual way.

## I. FUCHSIN-METHYL-BLUE

The best results are obtained after the above fixation. Zenker's fluid or formalin may be used. Bouin's fluid we have found less satisfactory. The fuchsin stains the eosinophil granules more brilliantly than the eosin of the second method and is preferable especially for

demonstrating the fine granules in the cells of the hypophysis of pregnancy.

1. Wash in water.
2. 15 seconds to 2 minutes, or longer, in a freshly prepared 1 per cent solution of permanganate of potassium.
3. Wash in water.
4. The same time as used in (2) in 5 per cent aqueous oxalic acid.
5. Wash well, followed by washing in distilled water.
6. Stain with 5 per cent aniline acid fuchsin at 60°C.
   Heat the stain gently on the slide until it steams, not boils, and allow to cool for 6 to 10 minutes.
   The dye can be poured back into the bottle and used again. We have found with Lee that in the preparation of this solution, Altmann's aniline fuchsin, not more than 5 to 7 grams of fuchsin will dissolve in 100 c.c. of aniline water. The 20 grams of the usual formula are a waste of dye.
7. Wash in distilled water. If too red, the section may be decolorized somewhat by dipping once or twice in 95 per cent alcohol.
8. 5 to 10 minutes in a 0.05 per cent aqueous solution of methyl-blue (not methylene-blue) until the basophil cells can be distinctly seen.
9. Differentiate quickly in absolute alcohol; clear and mount.

The eosinophil granules stain bright red, the basophil deep blue. The purpose of the treatment with permanganate and oxalic acid (steps 2 to 4) is twofold. First, it prevents the staining of mitochondria which in the majority of autopsies presents no problem. In the second place, when the right time is hit upon, neither the fuchsin nor the methyl-blue stains the cytoplasm of the chromophobe cells and the connective tissue, except with a faint tinge of color. The length of treatment depends upon the freshness of the tissue and the promptness and thoroughness of the fixation. The fresher the tissue and the better the fixation, the longer the time required in (2) and (4). With a little practice only one trial section need be wasted. It is best for the average case to start with a time of about 30 seconds. If the eosinophil cells are too red and the connective tissue tends to stain red, increase the time; if the eosinophil cells are faint and the basophils too dark, together with a blue staining of the connective tissue, decrease the time. In a few instances, when the hypophysis was removed some time after death and probably fixed in one piece, we have found it better to omit steps 2 to 4 completely. The permanganate solution

deteriorates rather rapidly and after two days at most no longer approximates a one per cent solution. A five per cent stock solution keeps indefinitely.

### II. EOSIN-METHYL-BLUE

Fix the tissue in Helly's fluid as above. Zenker's fluid, formalin, or Bouin's can be used.

1. Wash in water.
2. Stain 2 to 12 hours in Mann's stain
   1 per cent aqueous eosin (water soluble yellowish), 35 cc.
   1 per cent aqueous methyl-blue, 35 cc.
   Water, 100 cc.
3. Wash in water.
4. Differentiate in 95 per cent alcohol containing 2 drops of concentrated ammonia water to 50 cc. of alcohol.
5. Wash in several changes of 95 per cent alcohol to remove the alkali.
6. 30 seconds to 1 minute in water acidified with a few drops of glacial acetic acid.
7. Wash in water, dehydrate quickly in alcohols, clear in xylol and mount.

The eosinophil granules stain red, the basophil deep blue. The chromophobe cells and connective tissue are faint blue or almost colorless. The methyl-blue in the above method is an excellent nuclear stain.

The methyl-blue is scarcely decolorized at all by water or alcohol, but is readily removed by alkali. The ammoniated alcohol of the present method acts less vigorously than the sodium hydroxide of the original and the basophil granules are better differentiated, while the ammonia removes less of the eosin. The absolute alcohol of the early method can be replaced by 95 per cent without difference in the result. The blue dye turns red in an alkaline solution and is restored to the former color in an acid or neutral one. There is considerable variation in the rapidity of differentiation depending on the sample of dye and the age of the tissue. For material from which the blue is removed too readily, substitute in (4) water containing one drop of ammonia to 50 cc. of water, followed by (5), washing in water. Then proceed as above. The methyl-blue changed by alkali is more soluble in alcohol than in water.

On some tissues an excellent preparation can be obtained by simply

differentiating in alcohol, leaving out the alkaline solution. Or, by staining 10 minutes or longer until the basophil cells are distinctly blue under the microscope, and then passing through alcohol, successful results can be secured in other cases. However, the above somewhat longer method has been found the best. For very fresh tissue fuchsin can be used in place of eosin, a one per cent solution of acid fuchsin being prepared containing one-tenth per cent methyl-blue and substituting this for the Mann's stain in Method II. Its value is quite limited, as with other than the most favorable material the fuchsin is too rapidly removed. One can stain the nuclei and basophil cells first in methyl-blue solutions, differentiate in alkali, bring back the color with acid, and then stain in eosin, differentiating the eosin in water, just as a section is stained with haematoxylin and eosin. This has no particular advantage over the recommended method. When a similar procedure is attempted, counterstaining with fuchsin, the blue unfortunately is decolorized.

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## BOOK REVIEWS

*The Infant Welfare Movement in the 18th Century.* By ERNEST CAUFIELD, M.S., M.D. 1931. [With a foreword by George Frederic Still, M.A., M.D.] Illust. 203 Pp. $2.00. (*Paul B. Hoeber, Inc., New York.*)

Whoever has visited the Ospedâle degli innocenti in Florence will always remember Bronzino's lovely fresco, the massacre of the innocents, contrasting with the benevolence of the Florentine citadini in the care of the abandoned and poor children of the city, of whom it was said "Pater et mater reliquerunt nos, Dominus autem assumpsit—"

Dr. Caufield presents the same Bronzino contrasts in handling this phase of pediatric history. His first two chapters deal with the enormous infantile mortality resulting from carelessness; a story of "dropped" infants, of greedy, drunken nurses, of babies wasted by undernutrition and chronic digestive disturbance, quieted by opium or comatose, or by gin administered by their attendants. Still more horrible was the purposeful blinding and maiming of the infants carried about the country by beggars as incitants to sympathy and charity.

The other chapters are attractive sketches of the stories of Captain Coram, [whose name is perpetuated in the "Tattycoram" of Little Dorrit] and the Foundling Hospital, of Jonas Hanway and of Dr. Armstrong, for the last of whom Dr. Caufield has evidently a well-deserved admiration.

The book is well written and has an excellent bibliography, from which many quotations occur in the text.

P. G. S.

*The Youngest of the Family.* By JOSEPH GARLAND, M.D. 1932. 196 Pp. (*Harvard University Press, Cambridge, Mass.*)

This is one of the enormous family of booklets on the care and feeding of infants which has appeared during the last few years, and probably no better and no worse than any one of its generation. They are today the only recognized descendants from the days of Petrus Hispanus and Buchan. These popular manuals are all too sketchy and inaccurate to be of use to the physician, and serve only to perplex the primiparae who consult them, while advertising the author to the public.

P. G. S.

*The Advance of Medicine.* By the Right Honorable LORD MOYNIHAN, K.C., M.G., C.B. 1932. 64 Pp. [The Romanes Lecture.] Delivered in the Sheldonian Theatre, June 1, 1932. $1.00. (*Oxford, at the Clarendon Press.*)

This Romanes lecture is, in effect, a cultural handbook of the contributory factors in the making of medicine. It should prove a most enlightening and funda-

mental book to the student. The profit acquired by an hour's reading of it will be rewarding.

M. P.

*Chaucer and the Medieval Sciences.* By WALTER CLYDE CURRY. 1926. (*Oxford Univ. Press., New York.*)

Chaucer, like Dante, is replete with the scientific ideas of the middle ages. Curry has in a most illuminating way searched the Canterbury Tales for references to medieval science and more particularly medicine. The book is a delightful one, whether for study or recreation, and is undoubtedly the most informing presentation of the subject in English.

M. P.

*Poliomyelitis.* A survey made possible by a grant from the International Committee for the Study of Infantile Paralysis. Organized by Jeremiah Milbank. By various authors. 1932. 562 Pp. (*Williams & Wilkins Co. Balto., Md.*)

The actual authors are Miss Elizabeth Hutchins, Dr. Helen Harrington, Dr. Josephine B. Neal and Dr. Mildred Weeks Wells.

The book presents a summary of some 8,000 references and implies work of Gargantuan proportions which can be appreciated only by one who has done similar research. The bibliography covers 43 pages, in effect the cream of the enormous available material. The presentation is scholarly and well-arranged. The inclusion of a chapter on physiotherapy would have been a godsend both to physician and patient.

The historical chapter is an abridged account from the material in hand. In the section on resistance and immunity the subject of active immunization is intelligently handled as are the neutralizing substances and the immune sera.

Dr. Neal's classification covers the abortive, non-paralytic, subcortical paralysis, cerebral or encephalitic types of the disease and an atoxic type. A subheading of "meningitic type" would have facilitated the description given. The modalities of the disease are satisfactorily stated, but not in the fullest detail. There is a splendid account of the pathology, and the writer's consideration of the epidemiology leaves nothing to be desired.

The Milbank Committee may be congratulated on this, the best book on Poliomyelitis that has appeared to date. No one who has to cope with the disease can afford to be without it.

A similar book on treatment after the acute stage is over, with a more comprehensive consideration of "care and management" of the acute stage as well, as distinguished from scientific treatment, would fill a "long felt want." As a vademecum for the busy practitioner, the book may serve as a model.

J. R.

*The Heart Rate.* E. P. BOAS AND E. F. GOLDSCHMIDT. 1932. 166 pp. (*Chas. C. Thomas, Baltimore, Md.*)

Dr. Boas and his associates have developed a cardiatachometer, an instrument

that will give a continuous record of the pulse rate under any conditions. With this instrument they have studied the effect of sleep, exercise, surgical operations, disease and many other conditions on the pulse rate. The results are given in this book. More useful data on the pulse rate have been obtained by this method than by the discontinuous records of pulse rate taken during the past two hundred years.

C. L. G.

*Functional Disorders of the Gastro-Intestinal Tract.* By WILLIAM GERRY MORGAN, M.D., F.A.C.P. 1932. Illust. 259 pp. $5.00. [Everyday Practice Series.] Edited by Harlow Brooks. (*J. P. Lippincott Co., Phila., Pa.*)

This is, in all probability, the first book on the subject in English. Being intended for the busy practitioner, it offers no bibliographic or critical review of the literature and no references to experimentation.

The first part deals with the correlation of the nervous system and the function of digestion. The second covers the motor, secretory and sensory neuroses of the stomach separately. Gastro-intestinal dysfunction should of course be treated as a whole, not as of an organ or one phase of an organ's functions. Dr. Morgan recognizes this, in a manner, when he discusses the motor-secretory-sensory affections of the intestines as one. No detail is given nor is sufficient emphasis made of the psycho-biologic approach in history taking and as complementary to other forms of therapy, a procedure which the practitioner must acquire and use if he is to manage satisfactorily most of these cases.

The last part of the volume deals with constipation, flatulence, borborygmus and visceroptosis.

The book is clearly and simply written and contains an abundance of case reports with some detailed account as to therapeutic management. Incidentally, ulcerative colitis, an organic disease, is included.

M. P.

*The Failing Heart of Middle Life.* By ALBERT S. HYMAN AND AARON E. PARSONNET. With a Preface by David Riesman. 1932. 538 pp. $5.00. (*F. A. Davis Co., Phila.*)

The authors seek to distinguish between "the degenerative changes normally present in every individual reaching the half-way mark of his allotted span of life" and "the true diseases of the heart and blood vessels." They express dissatisfaction with the term "chronic myocarditis" and urge the substitution of the term "myocardosis," suggested by Riesman. Their thesis includes an elaborate, logical, consideration of diseases of the coronary arteries and angina pectoris. Pathology, clinical manifestations and therapy are adequately considered. Finally, there is a concise section upon the medicolegal aspects of sudden death from heart disease.

This volume should prove useful to student and physician. The bibliography is exhaustive—1250 titles—and would be more valuable if more closely linked with the text by key numbers.

In reviewing the "electrocardiographic changes in coronary disease" the authors very properly inveigh against the prevalent custom of attempting to make a clinico-pathologic diagnosis from tracings alone.

E. C. A.

*La Transplantation Animale.* By RAOUL M. MAY, Sc.D., Ph.D. 1932. 352 pp. 70 frs. (*Gauthiers-Villars, Paris.*)

This monograph affords a timely and comprehensive review of experimental morphology, now and for long a highly special, dramatic, and much labored field of investigation. The results of many widely scattered researches are here brought together and as far as possible correlated, in a masterly fashion. But, there is no attempt at forced conclusions; rather are the paradoxes clearly presented. Much is necessarily devoted to the amphibian embryo and its organization, including such involved questions as polarity, equipotentiality and regeneration. The opening chapter gives a cursory review of dissociation and regeneration in the invertebrates; the closing chapter treats briefly of neoplastic grafts. To each chapter a very adequate bibliography is appended.

C. F. D.

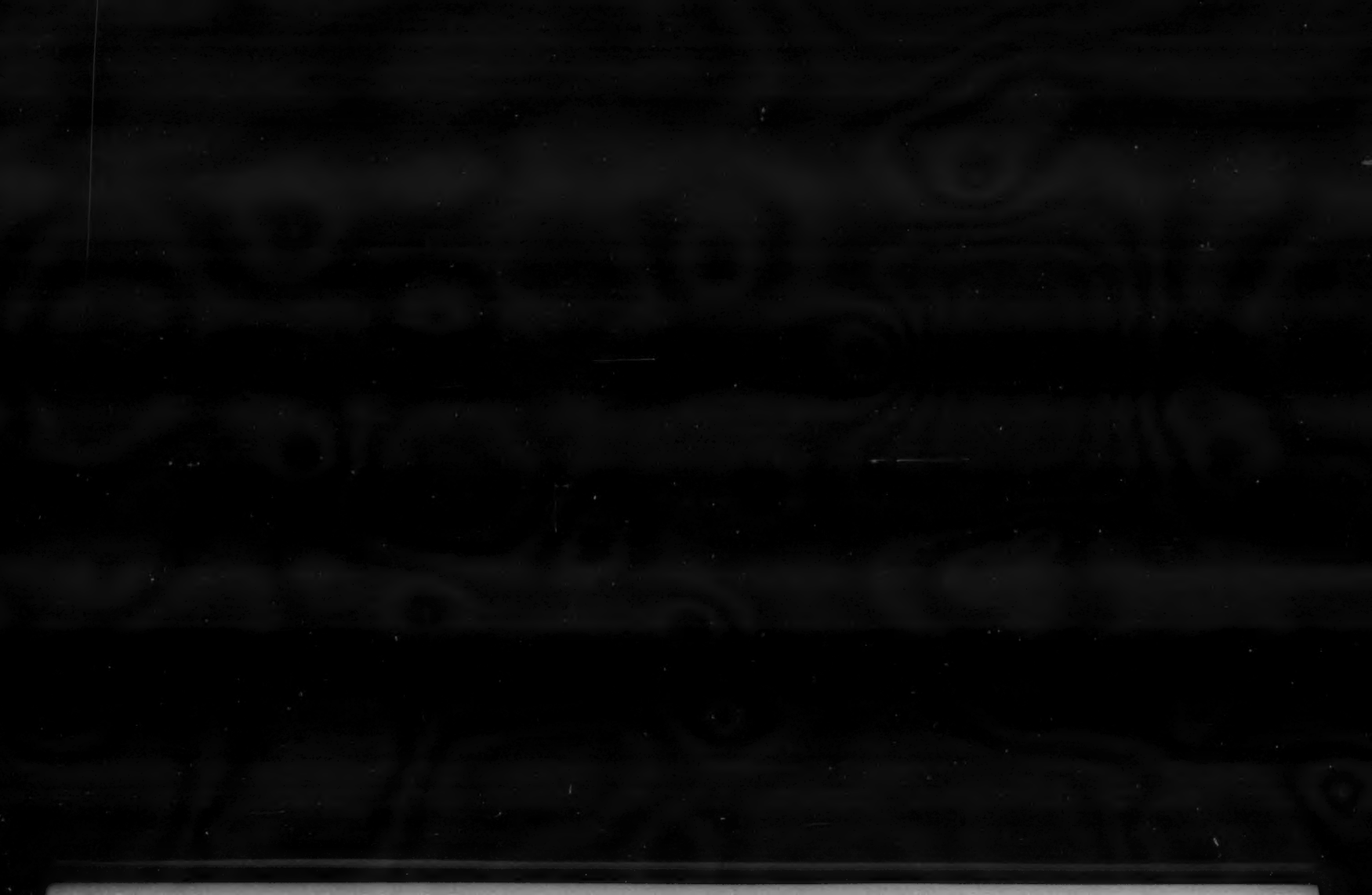
*Excitability. A Cardiac Study.* By W. BURRIDGE, D.M., M.A. 208 pp. index included, preface and table of contents. $3.85. (*Oxford University Press, New York, 1932.*)

*A New Physiology of Sensation. Based on a Study of Cardiac Action.* By W. BURRIDGE, D.M., M.A. 1932. Pp. 70, index included, preface and table of contents. $1.50. (*Oxford University Press, New York, 1932.*)

These books written in essay form may be considered together, for the argument in the second is based on premises developed in the first. Indeed had the matter of the two been arranged for one volume, much repetition would have been avoided and the cost of publication cut down considerably. Both books deal with the fundamental factors underlying excitation, conduction and response. Pharmacologist and cardiologist will find matter of interest in the first; psychologist and psychiatrist in the second. The essays show an unusual degree of originality and independence.

C. D. S.

*Pulmonary Tuberculosis.* By MAURICE FISHBERG, M.D. 1932. 4th Edit. Thoroughly revised. Vols. I & II. 1191 pp. $15.00. (*Lea & Febiger, Phila., Pa.*)

From the student's point of view, a great deal may be learned about the clinical aspect of pulmonary tuberculosis through reading this comprehensive text. The addition of many roentgenographic plates makes the new edition very valuable indeed.

D. S.